

L3 ANSWER 1 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95841 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: WO 2000047741 A1 20000817 156p

APPLICATION INFO: WO 2000-US3652 20000211

PRIORITY INFO: US 1999-249675 19990212

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a modified human erythropoietin signal peptide having at its C-terminus the **pro sequence** from human serum albumin. The invention is directed to glycosylated leptin proteins (see Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802), with Val-1 substituted by Ala, was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 4 in COS host cells and 4 in CHO cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 2 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95840 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: WO 2000047741 A1 20000817 156p

APPLICATION INFO: WO 2000-US3652 20000211

PRIORITY INFO: US 1999-249675 19990212

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a modified human erythropoietin signal peptide having at its C-terminus a modified **pro sequence** from NT-3. The invention is directed to glycosylated leptin proteins (see Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802) was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 3.5 in COS host cells and 3 in CHO cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 3 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95839 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: WO 2000047741 A1 20000817 156p

APPLICATION INFO: WO 2000-US3652 20000211

PRIORITY INFO: US 1999-249675 19990212

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a modified human erythropoietin signal peptide having at its C-terminus a modified **pro sequence** from human serum albumin, and co-expressed with furin. The invention is directed to glycosylated leptin proteins (see

Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802) was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 4 in COS host cells and 4.5 in CHO cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 4 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95838 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: WO 2000047741 A1 20000817 156p

APPLICATION INFO: WO 2000-US3652 20000211

PRIORITY INFO: US 1999-249675 19990212

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a modified human erythropoietin signal peptide having at its C-terminus a modified **pro sequence** from human serum albumin. The invention is directed to glycosylated leptin proteins (see Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802) was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 4 in COS host cells and 4.5 in CHO cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 5 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95837 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: WO 2000047741 A1 20000817 156p

APPLICATION INFO: WO 2000-US3652 20000211

PRIORITY INFO: US 1999-249675 19990212

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a modified human erythropoietin signal peptide having at its C-terminus the **pro sequence** from human serum albumin. The invention is directed to glycosylated leptin proteins (see Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802) was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 4 in COS host cells and 4.5 in CHO cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 6 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000P-Y95806 Peptide DGENE

TITLE: Glycosylated leptin proteins having a Stokes' radius greater than that of a naturally occurring glycosylated human leptin useful for treating obesity, diabetes and the effects of high blood lipid content -

INVENTOR: Martin F H; Elliott S G
 PATENT ASSIGNEE: (AMGE-N)AMGEN INC
 PATENT INFO: WO 2000047741 A1 20000817 156p
 APPLICATION INFO: WO 2000-US3652 20000211
 PRIORITY INFO: US 1999-249675 19990212
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-524540 [47]

AB The present sequence is that of a human leptin signal peptide that is the same as the native signal peptide, with the addition of a '**pro**' **sequence** (Arg-Gly-Arg-Phe-Arg-Arg) at the C-terminus. The invention is directed to glycosylated leptin proteins (see Y95799-804) that have a Stokes' radius greater than that of naturally occurring human leptin. A claimed method for manufacturing a glycosylated leptin involves culturing a host cell containing a DNA sequence encoding a signal peptide and a glycosylated leptin protein. Preferred signal peptides have a peptidase cleavage site optimized for glycosylation efficiency. When leptin+47+69+102 (see Y95802) was expressed as a **fusion** with the present signal peptide, the degree of glycosylation (on a scale of 1-5) was 3 in COS host cells and 4.5 in CHO host cells. Glycosylated leptins, or nucleic acids encoding them, are used in the treatment of obesity, diabetes and the effects of high blood lipid content (claimed). They have longer systemic circulation times in vivo than native leptins

L3 ANSWER 7 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1999P-Y28822 peptide DGENE
 TITLE: Novel methods for the secretion of glycosylated proteins used in the recombinant production and extracellular recovery of chimeric or **fusion** proteins -
 INVENTOR: Ashkenazi A J; Berman P W; Brousseau D; Etcheverry T
 PATENT ASSIGNEE: (GETH)GENENTECH INC
 PATENT INFO: WO 9953059 A1 19991021 47p
 APPLICATION INFO: WO 1999-US8110 19990414
 PRIORITY INFO: US 1998-82002 19980416
 US 1999-123522 19990308
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1999-611302 [52]

AB The present sequence is a **fusion** protein comprising human tissue plasminogen activator (tPA) **pro-sequence** and tumour necrosis factor (TNFR1) signal sequence. It can be produced from a DNA construct generated by operably linking tPA **pro-sequence** gene to the gene encoding endogenous signal sequence of tumour necrosis factor immunoglobulin chimera (TNFR1-IgG1). TNFR1-IgG1 used is a glycosylation site deletion variant. Chinese hamster ovary (CHO) cells are transformed with expression vectors containing the DNA construct and cultured for the production of TNFR1-IgG1 mutant polypeptide, whose secretion efficiency is greatly enhanced. Improved intracellular transport and recovery of immunoadhesins, like TNFR1-IgG1 with poor secretion kinetics, can be effected by this method

L3 ANSWER 8 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1999P-Y28821 peptide DGENE
 TITLE: Novel methods for the secretion of glycosylated proteins used in the recombinant production and extracellular recovery of chimeric or **fusion** proteins -
 INVENTOR: Ashkenazi A J; Berman P W; Brousseau D; Etcheverry T
 PATENT ASSIGNEE: (GETH)GENENTECH INC
 PATENT INFO: WO 9953059 A1 19991021 47p
 APPLICATION INFO: WO 1999-US8110 19990414
 PRIORITY INFO: US 1998-82002 19980416
 US 1999-123522 19990308
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1999-611302 [52]

AB The present sequence is a human tissue plasminogen activator (tPA) **pro-sequence**. It is obtained from tPA precursor peptide upon removal of signal sequence by cleavage with signal peptidase. A DNA construct can be generated by operably linking tPA **pro-sequence** gene to the gene encoding a heterologous glycoprotein, tumour necrosis factor immunoglobulin chimera (TNFR1-IgG1). TNFR1-IgG1 used is a glycosylation site deletion variant. Chinese hamster ovary (CHO) cells are transformed with expression vectors containing the DNA construct and cultured for the production of TNFR1-IgG1 mutant polypeptide, whose secretion efficiency is greatly enhanced. Improved intracellular transport and recovery of immunoadhesins, like TNFR1-IgG1 with poor secretion kinetics, can be effected by this method

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ACCESSION NUMBER: 1999P-Y28820 peptide DGENE

TITLE: Novel methods for the secretion of glycosylated proteins used in the recombinant production and extracellular recovery of chimeric or **fusion** proteins -

INVENTOR: Ashkenazi A J; Berman P W; Brousseau D; Etcheverry T

PATENT ASSIGNEE: (GETH)GENENTECH INC

PATENT INFO: WO 9953059 A1 19991021 47p

APPLICATION INFO: WO 1999-US8110 19990414

PRIORITY INFO: US 1998-82002 19980416

US 1999-123522 19990308

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1999-611302 [52]

AB The present sequence is a human tissue plasminogen activator (tPA) **pro-sequence**. It is obtained from tPA precursor peptide upon removal of signal sequence by cleavage with signal peptidase. A DNA construct can be generated by operably linking tPA **pro-sequence** gene to the gene encoding a heterologous glycoprotein, tumour necrosis factor immunoglobulin chimera (TNFR1-IgG1). TNFR1-IgG1 used is a glycosylation site deletion variant. Chinese hamster ovary (CHO) cells are transformed with expression vectors containing the DNA construct and cultured for the production of TNFR1-IgG1 mutant polypeptide, whose secretion efficiency is greatly enhanced. Improved intracellular transport and recovery of immunoadhesins, like TNFR1-IgG1 with poor secretion kinetics, can be effected by this method

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ACCESSION NUMBER: 1999P-Y28818 peptide DGENE

TITLE: Novel methods for the secretion of glycosylated proteins used in the recombinant production and extracellular recovery of chimeric or **fusion** proteins -

INVENTOR: Ashkenazi A J; Berman P W; Brousseau D; Etcheverry T

PATENT ASSIGNEE: (GETH)GENENTECH INC

PATENT INFO: WO 9953059 A1 19991021 47p

APPLICATION INFO: WO 1999-US8110 19990414

PRIORITY INFO: US 1998-82002 19980416

US 1999-123522 19990308

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1999-611302 [52]

AB The present sequence is a human tissue plasminogen activator (tPA) signal/**pro peptide**. A DNA construct can be generated by operably linking tPA gene to the gene encoding a heterologous glycoprotein, tumour necrosis factor immunoglobulin chimera (TNFR1-IgG1). TNFR1-IgG1 used is a glycosylation site deletion variant. Chinese hamster ovary (CHO) cells are transformed with expression vectors containing the DNA construct and cultured for the production of TNFR1-IgG1 mutant polypeptide, whose secretion efficiency is greatly enhanced. Improved intracellular transport and recovery of immunoadhesins, like TNFR1-IgG1 with poor secretion kinetics, can be effected by this method

L3 ANSWER 11 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1999P-W87637 Protein DGENE

TITLE: Preparation of recombinant polypeptides - by expression of a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen and a heterologous polypeptide

INVENTOR: Alcantara J; Moloney M; Van Rooijen G

PATENT ASSIGNEE: (SEMB-N)SEMBIOSYS GENETICS INC

PATENT INFO: WO 9849326 A1 19981105 44p

APPLICATION INFO: WO 1998-CA398 19980423

PRIORITY INFO: US 1997-44254 19970425

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1999-059646 [05]

AB The present sequence represents a **fusion** protein comprising a His tag-bovine chymosin **pro-peptide**-carp growth hormone. The **fusion** protein was made to exemplify the invention. The specification describes a method for preparing a recombinant polypeptide in a host cell. A chimeric nucleic acid sequence encoding a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen linked a protein heterologous to the **pro-peptide**, is introduced into the host cell. The host cells are then grown to produce the **fusion** protein. Altering the environment of the **fusion** protein allows cleavage of the **pro-peptide** from the **fusion** protein to release the recombinant polypeptide. The method can be used for the preparation of

recombinant polypeptides such as hirudin or carp growth hormone. The **fusion** proteins can be used for delivering to a human or animal a therapeutic or nutritional polypeptide such as a vaccine, a peptide antibiotic, a cattle feed enzyme, a cytokine, a gastric lipase or a lactase

L3 ANSWER 12 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1999P-W87636 Protein DGENE
 TITLE: Preparation of recombinant polypeptides - by expression of a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen and a heterologous polypeptide
 INVENTOR: Alcantara J; Moloney M; Van Rooijen G
 PATENT ASSIGNEE: (SEMB-N)SEMBIOSYS GENETICS INC
 PATENT INFO: WO 9849326 A1 19981105 44p
 APPLICATION INFO: WO 1998-CA398 19980423
 PRIORITY INFO: US 1997-44254 19970425
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1999-059646 {05}

AB The present sequence represents a **fusion** protein comprising glutathione-S-transferase (GST)-bovine chymosin **pro-peptide**-leech hirudin. The chymosin **pro-peptide** sequence is placed upstream of the DNA sequence encoding the leech anticoagulant protein hirudin. The **fusion** protein was made to exemplify the invention. The specification describes a method for preparing a recombinant polypeptide in a host cell. A chimeric nucleic acid sequence encoding a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen linked a protein heterologous to the **pro-peptide**, is introduced into the host cell. The host cells are then grown to produce the **fusion** protein. Altering the environment of the **fusion** protein allows cleavage of the **pro-peptide** from the **fusion** protein to release the recombinant polypeptide. The method can be used for the preparation of recombinant polypeptides such as hirudin or carp growth hormone. The **fusion** proteins can be used for delivering to a human or animal a therapeutic or nutritional polypeptide such as a vaccine, a peptide antibiotic, a cattle feed enzyme, a cytokine, a gastric lipase or a lactase

L3 ANSWER 13 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1998P-W64068 Protein DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor
 INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212
 PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 {30}

AB This sequence represents a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human insulin-like growth factor, IGF-I-A, as well as a human IGF propeptide. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 14 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1998P-W64066 Protein DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor
 INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212

PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 [30]

AB This sequence represents a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human platelet derived growth factor type B (PDGF-B) and also contains a human propeptide sequence and an ADH/GAP promoter. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 15 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998P-W64064 Protein DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor

INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212
 PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 [30]

AB This sequence represents a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human platelet derived growth factor type B (PDGF-B) and also contains a human propeptide sequence. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 16 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998P-W59044 protein DGENE
 TITLE: Recombinant yeast that secretes alpha-acetolactate decarboxylase - useful for making beer

INVENTOR: Goelling D; Moench J; Stahl U
 PATENT ASSIGNEE: (BIOT-N)BIOTECOM-GES BIOTECHNOLOGISCHE
 PATENT INFO: DE 19641569 A1 19980416 12p
 APPLICATION INFO: DE 1996-19641569 19961009
 PRIORITY INFO: DE 1996-19641569 19961009
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 OTHER SOURCE: 1998-231485 [21]

AB This protein sequence represents a **fusion** protein composed of a **pre-pro sequence** from yeast alpha-factor (MF-alpha) fused to a yeast alpha-acetolactate decarboxylase (ALDC) protein fragment. This protein is used in the production of a novel type of brewers yeast. The yeast secretes ALDC into the brewing medium. The secreted ALDC converts alpha-acetolactate into acetoin, thus circumventing formation of diacetyl and reducing generation of an undesirable buttery taste in the beer

L3 ANSWER 17 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995P-R74225 Protein DGENE
 TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
 PATENT ASSIGNEE: (GEMV)GENENCOR INC
 PATENT INFO: US 5411873 A 19950502 32p
 APPLICATION INFO: US 1984-614612 19840529
 PRIORITY INFO: US 1986-846627 19860401
 US 1984-614612 19840529

US 1990-488433 19900227
US 1992-928697 19920811

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB The amino acid sequence of the *Bacillus subtilis* subtilisin protein. The gene is used in a method to produce a carbonyl hydrolase (subtilisin) e.g. the *B.amyloliquefaciens* subtilisin (Q90041) or other heterologous protein (produced as a **fusion** protein) e.g. human growth hormone, such that the desired protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B.subtilis* subtilisin or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The *B.amyloliquefaciens* sequence was mutated using the primers Q90044-5 and Q*****-, specifically at S221N, D32N, A48R or contained a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 18 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995P-R74224 Protein DGENE
TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**
INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB The amino acid sequence of the *Bacillus subtilis* subtilisin protein. The gene is used in a method to produce a carbonyl hydrolase (subtilisin) e.g. the *B.amyloliquefaciens* subtilisin (Q90041) or other heterologous protein (produced as a **fusion** protein) e.g. human growth hormone, such that the desired protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B.subtilis* subtilisin or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The *B.amyloliquefaciens* sequence was mutated using the primers Q90044-5 and Q*****-, specifically at S221N, D32N, A48R or contained a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 19 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995P-R74223 Protein DGENE
TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**
INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB The amino acid sequence of the *Bacillus amyloliquefaciens* subtilisin. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B.subtilis* subtilisin (Q90042) or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The *B.amyloliquefaciens* sequence was mutated using the primers Q90044-5 and Q*****-, specifically at S221N, D32N, A48R or a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 20 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995P-R70264 Protein DGENE
TITLE: Secretion sequence for prodn. of a heterologous protein in yeast - useful for the expression of insulin-like growth factor-1
INVENTOR: Brierley R A; Howland D S; Scott R W
PATENT ASSIGNEE: (CEPH-N)CEPHALON INC
PATENT INFO: WO 9507978 A 19950323 80p
APPLICATION INFO: WO 1994-US9653 19940824
PRIORITY INFO: US 1993-122889 19930916
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-131346 [17]
AB This **fusion** protein (partial sequence only) is derived from the PKD template DNA. PKD is a template DNA (partial sequence shown here) for a **fusion** gene contg. the coding sequences for human insulin-like growth factor-I (IGF-I) and peptide sequences necessary for secretion of the protein, ie. the PHO signal peptide, which in PKD and all other recombinant templates contg. the acid phosphatase signal sequence, an L to F substitution at amino acid 6 of the signal peptide was made by changing codon CTA (present in native PHO sequence) to TCC. PKD contains the same **pro sequence** as PKV (R70263) but with a V to D substitution to possibly enhance cleavage at the neighbouring KR sequence. The recombinant DNA is used to express a protein in yeast cells. The signal peptide ensures secretion of the heterologous protein which can then be isolated from the yeast cell culture supernatant. The DNA sequence can also be used to determine the ability of a secretory facilitating element, ie. the K. lactis killer toxin precursor protein as in this sequence, or signal peptide to direct secretion of a protein from a yeast host. The element is inserted into the DNA and can be assayed. See also R70262-70

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YOU HAVE REQUESTED DATA FROM 123 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 21 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995P-R63864 peptide DGENE
TITLE: New **fusion** polypeptide(s) and glycosylation inhibition factor - used to develop prods. for suppressing an undesirable response, partic. allergies and auto:immune disease
INVENTOR: Ishizaka K; Liu Y; Mikayama T
PATENT ASSIGNEE: (KIRI)KIRIN BEER KK
(LJOL-N) LA JOLLA INST ALLERGY & IMMUNOLOGY
PATENT INFO: WO 9426923 A 19941124 156p
APPLICATION INFO: WO 1994-US5354 19940513
PRIORITY INFO: US 1993-61041 19930514
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-006814 [01]
AB A pure **fusion** polypeptide of the formula in R63864 is claimed. Specifically claimed are **fusion** polypeptides where the carrier peptide is derived from the **pro-region** of calcitonin precursor, and the polypeptide encoded by the structural gene is murine or human antigen non-specific glycosylation inhibiting factor (GIF). In eukaryotes, the carrier peptide transports the **fusion** polypeptide across the endoplasmic reticulum. The secretory protein is then transported through the Golgi apparatus into secretory vesicles and into the extracellular space or the external environment. The cleavage site allows for a high level of active protein encoded by the structural gene to be produced

L3 ANSWER 22 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994P-R60616 Protein DGENE
TITLE: New multimeric polypeptide comprising fused subunits of natural protein. - and related DNA and transformed cells, esp. dimers of platelet derived growth factor, useful for stimulating healing of wounds
INVENTOR: Thomason A R
PATENT ASSIGNEE: (AMGE-N)AMGEN INC
PATENT INFO: EP 618227 A 19941005 30p
APPLICATION INFO: EP 1994-105075 19940331
PRIORITY INFO: US 1993-41635 19930401
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-304405 [38]
AB The PDGF-B 109 subunit coding sequence was obtained as composite sequence of fragments from human PDGF-B pre-**pro region**, human v-sis gene and synthetic fragments. The mature 109 amino acid subunit was

incorporated into a single polypeptide with a PDGF-B 119 subunit, separated by a peptide linker to produce the preferred **fusion** polypeptide of the invention (R60616). The **fusion** dimer is more easily and rapidly refolded than unfused multimers and is useful for treating wounds

L3 ANSWER 23 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R60615 Protein DGENE

TITLE: New multimeric polypeptide comprising fused subunits of natural protein. - and related DNA and transformed cells, esp. dimers of platelet derived growth factor, useful for stimulating healing of wounds

INVENTOR: Thomason A R

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: EP 618227 A 19941005 30p

APPLICATION INFO: EP 1994-105075 19940331

PRIORITY INFO: US 1993-41635 19930401

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-304405 [38]

AB The PDGF-B 109 subunit coding sequence was obtained as composite sequence of fragments from human PDGF-B pre-**pro region**, human v-sis gene and synthetic fragments. The mature 109 amino acid subunit was incorporated into a single polypeptide with a PDGF-B 119 subunit, pref. separated by a peptide linker to produce a preferred **fusion** polypeptide of the invention. The **fusion** polypeptide is useful for treating wounds

L3 ANSWER 24 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R59805 Protein DGENE

TITLE: Eukaryotic cutinase variants with improved lipolytic activity - with modified amino acid structure to improve compatibility with anionic surfactants

INVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
T W M; Verrips C T

PATENT ASSIGNEE: (UNIL)UNILEVER NV

(UNIL) UNILEVER PLC

PATENT INFO: WO 9414964 A 19940707 72p

APPLICATION INFO: WO 1993-EP3551 19931209

PRIORITY INFO: EP 1992-204079 19921223

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* *exlA*. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the *exlA* pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the *exlA* pre- sequence is fused with the N-terminal residue of mature cutinase. Cassette 7 is identical with cassette 6, but here the N-terminal residue of the encoded mature cutinase polypeptide has been changed from the original G to S in order to better fit the requirements for cleavage of the signal peptide. Cassettes 5,6 and 7 were assembled from the synthetic oligos

L3 ANSWER 25 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R59804 Protein DGENE

TITLE: Eukaryotic cutinase variants with improved lipolytic activity - with modified amino acid structure to improve compatibility with anionic surfactants

INVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
T W M; Verrips C T

PATENT ASSIGNEE: (UNIL)UNILEVER NV

(UNIL) UNILEVER PLC

PATENT INFO: WO 9414964 A 19940707 72p

APPLICATION INFO: WO 1993-EP3551 19931209

PRIORITY INFO: EP 1992-204079 19921223

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* *exlA*. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in

which the coding sequence for the ex1a pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the ex1a pre- sequence is fused with the N-terminal residue of mature cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 26 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R59803 Protein DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - with modified amino acid structure to improve compatibility
 with anionic surfactants
 INVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
 T W M; Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414964 A 19940707 72p
 APPLICATION INFO: WO 1993-EP3551 19931209
 PRIORITY INFO: EP 1992-204079 19921223
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* ex1A. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the ex1a pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 5 this connection is made by fusing the ex1a pre-sequence to the **pro-sequence** of cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 27 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R59800 Protein DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Van D E R ;
 Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* ex1A. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the ex1a pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the ex1A pre- -sequence is fused with the N-terminal residue of mature cutinase. Cassette 7 is identical with cassette 6, but here the N-terminal residue of the encoded mature cutinase polypeptide has been changed from the original G to S in order to better fit the requirements for cleavage of the signal peptide. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 28 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R59799 Protein DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Verrips C T;
 Van D E R
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in

Aspergillus niger var. awamori, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of A. niger var. awamori exlA. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the exlA pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the exlA pre- -sequence is fused with the N-terminal residue of mature cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 29 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R59798 Protein DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Van D E R ;
 Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic Fusarium solani pisi cutinase gene in Aspergillus niger var. awamori, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of A. niger var. awamori exlA. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the exlA pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 5 this connection is made by fusing the exlA pre-sequence to the **pro-sequence** of cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 30 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R59781 Peptide DGENE
 TITLE: Enzyme-contg. detergent compsns. - comprises anionic-nonionic
 surfactant system, and a lipolytic enzyme pref. a fungal
 cutinase derived from F. solani pisi
 INVENTOR: Hondmann D H A; Klugkist J; Marugg J D; Musters W; Van der
 Hijden H T W M; Warr J F
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9403578 A 19940217 67p
 APPLICATION INFO: WO 1993-EP1923 19930720
 PRIORITY INFO: GB 1992-16387 19920731
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-065669 [08]

AB This sequence is encoded by cassette 5 which was used in the expression of the Fusarium solani pisi cutinase gene in Aspergillus niger. This sequence contains the A. niger strong inducible exlA promoter and the cutinase **pro-sequence** N-terminal. The F. solani pisi cutinase gene was used in the production of the cutinase enzyme for use in an enzymatic detergent composition. The composition also comprises (by wt.) 0.1-50% of a surfactant system comprising 0-95% of 1 or more anionic surfactants and 5-100% of 1 or more nonionic surfactants. The composition exhibits a substantial lipolytic activity during the main cycle of a wash process in an automatic washing machine, and consequently produces lipolytic activity when used to wash fabrics which have not been in contact with the detergent product before. The composition is also especially suitable for use in combination with a tumble drier

L3 ANSWER 31 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994P-R57283 Protein DGENE
 TITLE: New nucleic acid encoding enterokinase activity - and related
 vectors, host cells, expression products and antibodies are
 useful in treating digestive disorders and for cleaving
fusion proteins
 INVENTOR: Lavallie E R
 PATENT ASSIGNEE: (GEMY)GENETICS INST INC
 PATENT INFO: WO 9416083 A 19940721 50p
 APPLICATION INFO: WO 1994-US616 19940113
 PRIORITY INFO: US 1993-5944 19930115
 DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-249229 [30]

AB The enterokinase (EK) (or the EK gene when used in gene therapy) is used to treat digestive disorders associated with low EK activity (esp. inability to process trypsinogen to trypsin). For cleaving **fusion** proteins, recombinant EK catalytic domain is much more efficient than the native two-chain holoenzyme and is not contaminated by other proteolytic enzymes. For expression of recombinant EK, the 1691-2398 DNA fragment was fused to the 3'-end of the signal peptide and **pro-region** of the human PACE gene. The prod. could be expressed in CHO cells to produce a chimaeric prod. from which the **pro-region** as cleaved by endogenous PACE, providing mature EK catalytic domain

L3 ANSWER 32 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R57133 Protein DGENE

TITLE: Cassette for expression and synthesis of mature heterologous protein in yeast - included pre sequence and **pro sequence** from an insect defensin precursor, also new expression vectors and transformed hosts

INVENTOR: Achstetter T

PATENT ASSIGNEE: (TRGE)TRANSGENE SA

PATENT INFO: EP 607080 A 19940720 39p

APPLICATION INFO: EP 1994-400062 19940111

PRIORITY INFO: FR 1993-171 19930111

DOCUMENT TYPE: Patent

LANGUAGE: French

OTHER SOURCE: 1994-226998 [28]

AB Expression vectors were constructed for recombinant expression of Ala-Pro-ovine trophoblastin in transformed yeast hosts. The vectors coded for a **fusion** of the presequence of yeast alpha 1- mating factor, the **pro sequence** of Phormia terranova defensin A and Ala-Pro-ovine trophoblastin, under the control of a modified alpha1-MF promoter. The recombinant proteins produced by yeast transformed with the vectors were isolated and sequenced at the N-terminus. R57133 is the N-terminal sequence of the desired recombinant heterologous protein

L3 ANSWER 33 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R57132 Protein DGENE

TITLE: Cassette for expression and synthesis of mature heterologous protein in yeast - included pre sequence and **pro sequence** from an insect defensin precursor, also new expression vectors and transformed hosts

INVENTOR: Achstetter T

PATENT ASSIGNEE: (TRGE)TRANSGENE SA

PATENT INFO: EP 607080 A 19940720 39p

APPLICATION INFO: EP 1994-400062 19940111

PRIORITY INFO: FR 1993-171 19930111

DOCUMENT TYPE: Patent

LANGUAGE: French

OTHER SOURCE: 1994-226998 [28]

AB Expression vectors were constructed for recombinant expression of the hirudin variant rHV2-Lys47 in transformed yeast hosts. The vectors coded for a **fusion** of the presequence of yeast alpha 1- mating factor, the **pro sequence** of Phormia terranova defensin A and rHV2-Lys47, under the control of the alpha1-MF promoter. The recombinant proteins produced by yeast transformed with the vectors were isolated and sequenced at the N-terminus. The chromatography profile of the culture products from one vector (which did not comprise the yeast KEX2 gene) showed two peaks. R57130 and R57131 are the N-terminal sequences of each peak. A different vector (additionally comprising the KEX2 gene) produced a single product having the N-terminal sequence R57132

L3 ANSWER 34 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994P-R57131 Protein DGENE

TITLE: Cassette for expression and synthesis of mature heterologous protein in yeast - included pre sequence and **pro sequence** from an insect defensin precursor, also new expression vectors and transformed hosts

INVENTOR: Achstetter T

PATENT ASSIGNEE: (TRGE)TRANSGENE SA

PATENT INFO: EP 607080 A 19940720 39p

APPLICATION INFO: EP 1994-400062 19940111

PRIORITY INFO: FR 1993-171 19930111

DOCUMENT TYPE: Patent

LANGUAGE: French

OTHER SOURCE: 1994-226998 [28]

AB Expression vectors were constructed for recombinant expression of the hirudin variant rHV2-Lys47 in transformed yeast hosts. The vectors coded for a **fusion** of the presequence of yeast alpha 1- mating factor, the **pro sequence** of Phormia terranova defensin A and rHV2-Lys47, under the control of the alpha1-MF promoter. The recombinant proteins produced by yeast transformed with the vectors were isolated and sequenced at the N-terminus. The chromatography profile of the culture products from one vector (which did not comprise the yeast KEX2 gene) showed two peaks. R57130 and R57131 are the N-terminal sequences of each peak. A different vector (additionally comprising the KEX2 gene) produced a single product having the N-terminal sequence R57132

L3 ANSWER 35 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994P-R57130 Protein DGENE
TITLE: Cassette for expression and synthesis of mature heterologous protein in yeast - included pre sequence and **pro sequence** from an insect defensin precursor, also new expression vectors and transformed hosts
INVENTOR: Achstetter T
PATENT ASSIGNEE: (TRGE)TRANSGENE SA
PATENT INFO: EP 607080 A 19940720 39p
APPLICATION INFO: EP 1994-400062 19940111
PRIORITY INFO: FR 1993-171 19930111
DOCUMENT TYPE: Patent
LANGUAGE: French
OTHER SOURCE: 1994-226998 [28]

AB Expression vectors were constructed for recombinant expression of the hirudin variant rHV2-Lys47 in transformed yeast hosts. The vectors coded for a **fusion** of the presequence of yeast alpha 1- mating factor, the **pro sequence** of Phormia terranova defensin A and rHV2-Lys47, under the control of the alpha1-MF promoter. The recombinant proteins produced by yeast transformed with the vectors were isolated and sequenced at the N-terminus. The chromatography profile of the culture products from one vector (which did not comprise the yeast KEX2 gene) showed two peaks. R57130 and R57131 are the N-terminal sequences of each peak. A different vector (additionally comprising the KEX2 gene) produced a single product having the N-terminal sequence R57132

L3 ANSWER 36 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993P-R37799 Protein DGENE
TITLE: Eukaryotic expression of neurotrophins - using prepro region of a different neurotrophin for more efficient post-translational processing
INVENTOR: Gies D; Hu S S; Ip N; Squinto S P; Yancopoulos G D
PATENT ASSIGNEE: (AMGE-N)AMGEN
(REGE-N) REGENERON PHARM INC
PATENT INFO: WO 9310150 A 19930527 80p
APPLICATION INFO: WO 1992-US9792 19921113
PRIORITY INFO: US 1991-792492 19911114
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-182492 [22]

AB This sequence represents human nerve growth factor (NGF). The protein encoded by this sequence promotes the development of the peripheral nervous system and also influences the development and maintenance of specific populations of neurons in the central nervous system. Two major transcripts from the NGF gene result in a "long" and "short" NGF prepropeptide. The "short" precursor contains a conventional signal sequence at the N-terminus which flanks the **pro-region**. The "long" precursor contains an additional **"pro-region"** at its N-terminal. No functional distinction has been elucidated between the "long" and "short" forms. Characteristics of NGF, such as isoelectric point and primary structure, are very similar to brain derived neurotrophic factor (BDNF). The NGF coding sequence may be used in the construction of a chimeric nucleic acid molecule to encode a prepro- NGF/BDNF chimera (see also Q42568-69)

L3 ANSWER 37 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992P-R21678 Protein DGENE
TITLE: Improved expression of peptide(s) as **fusion** proteins - using heterologous carrier with high isoelectric point for sepn. of peptide
INVENTOR: Tarnowski S J; Hilliker S; Willett W S
PATENT ASSIGNEE: (CALB-N)CALIF BIOTECHN INC
PATENT INFO: WO 9202550 A 19920220 50p
APPLICATION INFO: WO 1991-US5617 19910807
PRIORITY INFO: US 1990-564259 19900807

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-080032 [10]

AB This amino acid sequence is that of the human ANP **pro-sequence** but with all the Glu residues substituted with other amino acids so as to remove all Staph V8 cleavage sites. The proviso relating to residues 68 and 69 is to exclude an Asp-Gly cleavage site. The preferred amino acid for substitution of Glu at all these sites is Gln (see R21676 and R21677 for specific examples). The **pro-sequence** has a high isoelectric point (at least 8.0) which facilitates sepn. of the **pro-sequence** from the mature protein following cleavage. The modified human Pro-ANP sequence is the preferred "carrier protein" for use in the production of recombinant proteins, besides ANP, which can be fused to it

L3 ANSWER 38 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992P-R21677 Protein DGENE
TITLE: Improved expression of peptide(s) as **fusion** proteins - using heterologous carrier with high isoelectric point for sepn. of peptide
INVENTOR: Tarnowski S J; Hilliker S; Willett W S
PATENT ASSIGNEE: (CALB-N)CALIF BIOTECHN INC
PATENT INFO: WO 9202550 A 19920220 50p
APPLICATION INFO: WO 1991-US5617 19910807
PRIORITY INFO: US 1990-564259 19900807
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-080032 [10]

AB This **fusion** protein comprises the E.coli beta-gal leader peptide fused to pro-ANP. A Staph V8 protease cleavage site is present at the junction between the **pro-sequence** and the mature ANP sequence. Other cleavage sites in the protein were removed by changing the Glu residues in the **pro-sequence** to Gln residues. Human pro-ANP **pro-sequence** modified in this way is the preferred "carrier protein" for use in the production of other proteins, besides mature ANP. The carrier protein has a high isoelectric point which facilitates separation of the modified **pro-sequence** from these other proteins, e.g. somatostatin, calcitonin, insulin, bradykinins, enkephalins, brain natriuretic peptide, etc. See also Q21857 and R21678

L3 ANSWER 39 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992P-R21676 Protein DGENE
TITLE: Improved expression of peptide(s) as **fusion** proteins - using heterologous carrier with high isoelectric point for sepn. of peptide
INVENTOR: Tarnowski S J; Hilliker S; Willett W S
PATENT ASSIGNEE: (CALB-N)CALIF BIOTECHN INC
PATENT INFO: WO 9202550 A 19920220 50p
APPLICATION INFO: WO 1991-US5617 19910807
PRIORITY INFO: US 1990-564259 19900807
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-080032 [10]

AB This **fusion** protein comprises the E.coli beta-gal leader peptide fused to pro-ANP. Staph V8 protease cleavage sites are present at the junction between the leader and the **pro-sequence** and between the **pro-sequence** and the mature ANP sequence. Other cleavage sites in the protein were removed by changing the Glu residues in the **pro-sequence** to Gln residues. Human pro-ANP **pro-sequence** modified in this way is the preferred "carrier protein" for use in the production of other proteins, besides mature ANP. The carrier protein has a high isoelectric point which facilitates separation of the modified **pro-sequence** from these other proteins, e.g. somatostatin, calcitonin, insulin, bradykinins, enkephalins, brain natriuretic peptide, etc. See also Q21858 and R21678

L3 ANSWER 40 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992P-R21146 Protein DGENE
TITLE: Expression cassette contg. aprotinin gene and an AMF pre-**pro sequence** - contained in methylotrophic yeast, esp. Pichia pastoris, for large scale prodn. of aprotinin
INVENTOR: Vedvick T S; Engel M E; Can M S; Buckholz R G; Kinney J A
PATENT ASSIGNEE: (SALK)SALK INST BIOTECHN
PATENT INFO: WO 9201048 A 19920123 119p
APPLICATION INFO: WO 1991-US4744 19910703
PRIORITY INFO: US 1990-560618 19900730

US 1990-547985 19900703
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-056863 [07]

AB The peptide sequence is the N-terminus of an aprotinin protein produced by fermenting *P. pastoris* cells transformed with a recombinant gene encoding a **fusion** protein. The strain from run 731 produced an aprotinin analogue which had 6 amino acids attached to the N-terminus of the authentic aprotinin molecule. The addition of Glu-Ala sequences allowed for correct processing at the preceding Lys-Arg site, while one or more Glu-Ala residues remain at the N-terminus of the APR prod. Regardless of the additional amino acids at the N-terminus of APR, the analogue was seen to be highly bioactive. See also R21143,44

L3 ANSWER 41 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992P-R21144 peptide DGENE
TITLE: Expression cassette contg. aprotinin gene and an AMF pre-
pro sequence - contained in methylotrophic yeast, esp. *Pichia pastoris*, for large scale prodn. of aprotinin
INVENTOR: Vedvick T S; Engel M E; Can M S; Buckholz R G; Kinney J A
PATENT ASSIGNEE: (SALK)SALK INST BIOTECHN
PATENT INFO: WO 9201048 A 19920123 119p
APPLICATION INFO: WO 1991-US4744 19910703
PRIORITY INFO: US 1990-560618 19900730
US 1990-547985 19900703

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-056863 [07]

AB The peptide sequence is the N-terminus of an aprotinin protein produced by fermenting *P. pastoris* cells transformed with a recombinant gene encoding a **fusion** protein. The strain (G+APR205S10) produced an aprotinin analogue which had 11 amino acids attached to the N-terminus of the authentic aprotinin molecule. These 11 amino acids are from the carboxy terminus of the AMF leader sequence. This aprotinin analogue, secreted by the strain grown by fermentation, showed 100 percent bioactivity, i.e. the additional residues at the N-terminus did not interfere with activity. See also R21143,46

L3 ANSWER 42 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992P-R20634 Protein DGENE
TITLE: Nucleic acid sequences for production of CD4 chimeric protein - used to transfect *Streptomyces*, contg. LTI signal sequence linked to **pro-peptide** sequence facilitating peptide cleavage
INVENTOR: Brawner M E; Fornwald J A; Arthos J
PATENT ASSIGNEE: (SMIK)SMITHKLINE BEECHAM
PATENT INFO: WO 9200985 A 19920123 47p
APPLICATION INFO: WO 1991-US4663 19910701
PRIORITY INFO: US 1991-665218 19910305
US 1990-551584 19900711
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-056814 [07]

AB The sequence was deduced by sequencing the plasmid vector V1V2-hCH2- KA in *S. lividans* strain 1326. The protein has domains contg. peptides of different function. It contains a CD4 chimera (V1V2) in which the carboxy terminal portion of the protein consists of a murine immunoglobulin light chain constant region, linked to the signal peptide of *Streptomyces* LTI, modified at its N-terminus to include Lys-Arg. Also included is the IgG1 constant region comprising the hinge and CH2 motifs. Human IgG1 is the most effective immunoglobulin subclass at mediating cell killing by both complement and ADCC. The CD4 chimeric proteins may be expressed in bacterial hosts. The **fusion** of the human Ig constant region lacking the CH3 domain, and the LTI CD4 protein increases the stability of the CD4, thus increasing the serum half life and/or potency against HIV infection and inhibit virus-induced cell **fusion**, relative to soluble CD4. By altering only one amino acid at position 2 near the N terminal of CD4 (V1 region) from Lys to Ala, a heterologous protein is expressed which is efficiently secreted and correctly processed to remove the entire LTI signal sequence, but which still retains the gp120 binding capacity. By modifying the **pro-peptide** you avoid deleterious effects of additional amino acids on the function of the protein. See also R20635,6

L3 ANSWER 43 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992P-R20043 Protein DGENE
TITLE: Human osteocalcin prodn. - using DNA coding for human osteocalcin **fusion** protein for expression in host

cells
 INVENTOR: Eguchi H; Kamimura T F; Sugiyama T; Hosoda K
 PATENT ASSIGNEE: (TEIJ)TEIJIN KK
 PATENT INFO: EP 463571 A 19920102 53p
 APPLICATION INFO: EP 1991-110173 19910620
 PRIORITY INFO: JP 1990-330146 19901130
 JP 1990-159909 19900620
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1992-009183 [02]

AB This sequence is a specific example of a claimed generic **fusion** protein comprising human osteocalcin. The **pro-peptide** is recognised by an enzyme capable of Glu to Gla conversion on human osteocalcin. The recombinant protein was obtained by culturing host cells transformed with a vector containing the synthetic coding sequence. The Glu residues could then be converted to Gla (i.e. gamma-carboxyglutamic acid) and the osteocalcin sequence cleaved from the propeptide. The mature protein is suitable for use in immunoassays and as a drug for treatment of bone metabolism disorders. See also R20044-6

L3 ANSWER 44 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1991P-R13385 Protein DGENE
 TITLE: DNA constructs for secretion of foreign proteins - using signal sequence and portion of BAR1 C-terminal domain to direct secretion

INVENTOR: Welch S K; Mackay V L; Yip C L
 PATENT ASSIGNEE: (ZYMO-N)ZYMOGENETICS INC
 PATENT INFO: US 5037743 A 19910806 40p
 APPLICATION INFO: US 1988-270933 19881114
 PRIORITY INFO: US 1988-270933 19881114
 US 1987-104316 19871002
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-252061 [34]

AB By combining the Barrier protein signal sequence with amino acids 423-526 of the third (C-terminal) domain secretion levels for EGF greater than those obtd. using analogous constructs comprising the MEalphal **pre-pro sequence** are obtd. The hybrid secretory peptide directs the secretion of heterologous proteins or polypeptides, e.g. urokinase, insulin, platelet-derived growth factor, epidermal growth factor or transforming growth factor alpha. See also Q13195-7

L3 ANSWER 45 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1991P-R13384 Protein DGENE
 TITLE: DNA constructs for secretion of foreign proteins - using signal sequence and portion of BAR1 C-terminal domain to direct secretion

INVENTOR: Welch S K; Mackay V L; Yip C L
 PATENT ASSIGNEE: (ZYMO-N)ZYMOGENETICS INC
 PATENT INFO: US 5037743 A 19910806 40p
 APPLICATION INFO: US 1988-270933 19881114
 PRIORITY INFO: US 1988-270933 19881114
 US 1987-104316 19871002
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-252061 [34]

AB By combining the Barrier protein signal sequence with amino acids 391-526 of the third (C-terminal) domain secretion levels for TGF greater than those obtd. using analogous constructs comprising the MEalphal **pre-pro sequence** are obtd. The hybrid secretory peptide directs the secretion of heterologous proteins or polypeptides, e.g. urokinase, insulin, platelet-derived growth factor, epidermal growth factor or transforming growth factor alpha. See also Q13195-7

L3 ANSWER 46 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1991P-R12412 Protein DGENE
 TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia

INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
 PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
 (CHIR-N) CHIRON CORP
 PATENT INFO: WO 9107490 A 19910530 56p
 APPLICATION INFO: WO 1990-DK291 19901115
 PRIORITY INFO: US 1989-438639 19891117
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain (see Q12035). The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. In pSVF8-80A the Ser codon is changed to a Glu codon and 7 codons encoding the putative tPA **pro-peptide** are deleted. Cleavage by signal peptidase releases non-mutant FVIII:C light chain. This sequence corresponds to the **fusion** region as given in the specification with Val(11) and Leu(12) as found in the native tPA pre-**pro peptide**. The nucleotide sequence from which it was deduced, however, encodes Cys(11) and Val(12)

L3 ANSWER 47 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991P-R12411 Protein DGENE
TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia
INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
(CHIR-N) CHIRON CORP
PATENT INFO: WO 9107490 A 19910530 56p
APPLICATION INFO: WO 1990-DK291 19901115
PRIORITY INFO: US 1989-438639 19891117
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain (see Q12035). The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. In pSVF8-80R the Ser codon is changed to a Glu codon and the 3 codons corresponding to the tPA **pro-peptide** are deleted. This construction was made in the hope that cleavage by a Golgi-resistant protease with dibasic specificity would release FVIII:C light chains having Glu amino terminal. This sequence corresponds to the **fusion** region as given in the specification with Val(11) and Leu(12) as found in the native tPA pre-**pro peptide**. The nucleotide sequence from which it was deduced, however, encodes Cys(11) and Val(12)

L3 ANSWER 48 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991P-R12410 Protein DGENE
TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia
INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
(CHIR-N) CHIRON CORP
PATENT INFO: WO 9107490 A 19910530 56p
APPLICATION INFO: WO 1990-DK291 19901115
PRIORITY INFO: US 1989-438639 19891117
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain (see Q12035). The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. In pSVF8-80S the Ser codon is changed to a Glu codon and the 12 codons corresponding to amino acids -12 to -1 of the tPA pre-**pro-region** are deleted. Cleavage of the truncated signal peptide releases non-mutant FVIII:C light chain. This sequence corresponds to the **fusion** region as given in the specification with Val(11) and Leu(12) as found in the native tPA pre-**pro peptide**. The nucleotide sequence from which it was deduced, however, encodes Cys(11) and Val(12)

L3 ANSWER 49 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991P-R12409 Protein DGENE
TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia
INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
(CHIR-N) CHIRON CORP

PATENT INFO: WO 9107490 A 19910530 56p
 APPLICATION INFO: WO 1990-DK291 19901115
 PRIORITY INFO: US 1989-438639 19891117
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain (see Q12035). The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. In pSVF8-80KG the Ser codon is changed to a Glu codon to test whether the Arg-Glu protease could recognise and cleave the dipeptide in an altered context. This sequence corresponds to the **fusion** region as given in the specification with Val(11) and Leu(12) as found in the native tPA pre-**pro peptide**. The nucleotide sequence from which it was deduced, however, encodes Cys(11) and Val(12)

L3 ANSWER 50 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1991P-R12408 Protein DGENE
 TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia

INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
 PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
 (CHIR-N) CHIRON CORP

PATENT INFO: WO 9107490 A 19910530 56p
 APPLICATION INFO: WO 1990-DK291 19901115
 PRIORITY INFO: US 1989-438639 19891117
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain. The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. This sequence corresponds to the **fusion** region as given in the specification with Val(11) and Leu(12) as found in the native tPA pre-**pro peptide**. The nucleotide sequence from which it was deduced, however, encodes Cys(11) and Val(12)

L3 ANSWER 51 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1991P-R11726 Protein DGENE
 TITLE: Recombinant prodn. of CD4 in Pichia pastoris - where CD4 contains site of interaction between CD4 and HIV and is used to treat and prevent AIDS
 INVENTOR: Buckholz R G; Brierley R A; Odiorne M S; Siegel R S; Wondrack L M
 PATENT ASSIGNEE: (SALK)SALK INST BIOTECHN
 PATENT INFO: WO 9105057 A 19910418 64p
 APPLICATION INFO: WO 1990-US5520 19900927
 PRIORITY INFO: US 1989-413938 19890928
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-132862 [18]

AB An EcoRI-XbaI fragment was excised from a 2.2 kb linear BglII-NheI DNA fragment containing a segment encoding the first variable region of CD4 accompanied by flanking DNA from E.coli. The excised fragment was ligated to plasmid pIBI25 (containing an fl ORI and a T7 promoter) to give plasmid pSCD4. Digestion with XbaI and EcoRI showed a 477bp fragment contained the V1 region. This fragment was isolated and ligated to a plasmid containing the pre-**pro sequence** from yeast alpha-mating factor (AMF). Mutagenesis was performed to fuse the AMF pre-**pro sequence** directly to the V1 coding region. An EcoRI linker was added to the 3' end of the AMF pre-pro-V1 insert prior to digestion with EcoRI to give a 560bp fragment. The fragment was ligated to EcoRI-digested pAO815 (containing AOX1 transcription terminator) and the ligation mixture transformed into MC1061 cells. Plasmid pSCD103 was isolated from the transformants and the **fusion** protein it encodes has the sequence shown. See also Q11566

L3 ANSWER 52 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1989P-P92090 standard DGENE
 TITLE: Expression cassettes for enhanced polypeptide prodn. - having codon(s) modified using codon degeneracy to approximate those of Shine-Dalgarno sequence
 INVENTOR: Rose T M; Franceschini T J; Bruce A G; Liu S W

PATENT ASSIGNEE: (ONCO-N)Oncogen A Partn Ltd
 PATENT INFO: WO 8903886 A 19890505
 APPLICATION INFO: WO 1988-US3872 19881028
 PRIORITY INFO: US 1988-240768, 19880902
 DOCUMENT TYPE: Patent
 OTHER SOURCE: 1989-150782 [20]

AB Human EGF gene is expressed as part of a **fusion** with the 32 N-terminal amino acids of the N-gene. Treatment of the purified **fusion** protein with formic acid results in cleavage at the acid labile Asp-**Pro peptide** bond

L3 ANSWER 53 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1989P-P92085 standard DGENE
 TITLE: Expression cassettes for enhanced polypeptide prodn. - having codon(s) modified using codon degeneracy to approximate those of Shine-Dalgarno sequence
 INVENTOR: Rose T M; Franceschini T J; Bruce A G; Liu S W
 PATENT ASSIGNEE: (ONCO-N)Oncogen A Partn Ltd
 PATENT INFO: WO 8903886 A 19890505
 APPLICATION INFO: WO 1988-US3872 19881028
 PRIORITY INFO: US 1988-240768, 19880902
 DOCUMENT TYPE: Patent
 OTHER SOURCE: 1989-150782 [20]

AB The N-terminal sequence of the synthetic VGFA gene is a truncated version of the natural VGF sequence and begins with the sequence DIPAIR. Treatment of the purified **fusion** protein with formic acid results in cleavage at the acid labile Asp-**Pro peptide** bond allowing separation of the VGFA protein from the lambda N-protein amino-terminus. Cleavage is such that the VGFA protein is left with the proline residue at the amino terminus

L3 ANSWER 54 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1984P-P40025 Protein DGENE
 TITLE: Human insulin-like and epidermal growth factors - prepd. by cultivation of recombinant hosts
 INVENTOR: Lee J M; Ullrich A
 PATENT ASSIGNEE: (GETH)Genentech Inc
 PATENT INFO: EP 128733 A 19841219 68p
 APPLICATION INFO: EP 1984-303783 19840605
 PRIORITY INFO: US 1983-501353 19830606
 US 1983-506078 19830620
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1984-314109 [51]

AB The **fusion** protein comprises human insulin-like growth factor-1 (hIGF1) and alpha factor pre-**pro sequence**. The hIGF1 is cleaved from the **fusion** protein using the collagenase recognition site situated at the N-terminal of the mature hIGF1 sequence. The **fusion** protein is expressed by inserting the DNA into an expression vector and using this to transform a host cell. The hIGF1 is produced free from association with N-terminus amino acid sequences derivable from the expression systems used for its prepn. hIGF1 is useful for the prophylaxis or treatment of growth conditions

L3 ANSWER 55 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 2000N-Z90229 DNA DGENE
 TITLE: Producing peptides of high or low isoelectric point, particularly natriuretic peptides for treating congestive heart failure, by expression as cleavable **fusion** protein of nearly neutral isoelectric point -
 INVENTOR: Pollitt N S; Buckley D I; Stathis P A; Hartman T E; Zhong Z
 PATENT ASSIGNEE: (SCIO-N)SCIOS INC
 PATENT INFO: WO 2000003011 A2 20000120 40p
 APPLICATION INFO: WO 1999-US15147 19990708
 PRIORITY INFO: US 1998-92423 19980710
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-182222 [16]

AB The invention relates to the production of a peptide which has an isoelectric point (pI) below 5 or over 8. The peptide is expressed as a **fusion** protein (e.g., with a modified chloramphenicol acetyl transferase) in a host cell, and inclusion bodies containing the **fusion** protein are recovered. The **fusion** protein is cleaved under acidic conditions in the absence of a chaotrope, subsequently treated with a non-ionic chaotrope, and the desired peptide isolated by ion-exchange chromatography. The **fusion** partner protein has a C-terminal Asp - this Asp and the N-terminal amino acid of the desired peptide form a bond which can be cleaved under acid conditions. The **fusion** partner also promotes the formation of

inclusion bodies with the host cell, and has a net charge sufficiently different from that of the peptide and any unwanted cleavage fragments to allow separation of the peptide by ion-exchange chromatography. The invention also encompasses a variation of the method of the invention whereby chaotrope-mediated solubilisation is replaced by the removal of insoluble cleavage products by ultrafiltration, diafiltration or centrifugation; an expression vector encoding the **fusion** protein; and a host cell containing the vector. The method of the invention is specifically used to produce b-type natriuretic peptide (BNP, pI>10) which is useful for treating congestive heart failure. This peptide improves heart function without direct cardiac stimulation, which may cause arrhythmia, and decreases levels of neurohormones which are associated with increased mortality and acceleration of disease progression. Cleavage of the **fusion** protein in the absence of a chaotrope results in a soluble peptide which is easily separated from the other (insoluble) cleavage products for subsequent purification. Sequences Z90228-Z90229 represent PCR primers used in an exemplification of the invention to modify DNA encoding the wild-type BNP protein to produce DNA encoding a truncated version of BNP wherein the initial serine of the mature BNP was absent. The N-terminal residue of the truncated BNP is Pro; in the modified chloramphenicol acetyl transferase (CAT)/truncated BNP **fusion** protein, the CAT portion is linked to the BNP portion via an Asp-**Pro peptide** bond. The presence of the Asp-Pro bond facilitates liberation of BNP as acid cleavage occurs most rapidly at an Asp-**Pro peptide** bond

L3 ANSWER 56 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 2000N-Z90228 DNA DGENE
 TITLE: Producing peptides of high or low isoelectric point, particularly natriuretic peptides for treating congestive heart failure, by expression as cleavable **fusion** protein of nearly neutral isoelectric point -
 INVENTOR: Pollitt N S; Buckley D I; Stathis P A; Hartman T E; Zhong Z
 PATENT ASSIGNEE: (SCIO-N)SCIOS INC
 PATENT INFO: WO 2000003011 A2 20000120 40p
 APPLICATION INFO: WO 1999-US15147 19990708
 PRIORITY INFO: US 1998-92423 19980710
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-182222 [16]

AB The invention relates to the production of a peptide which has an isoelectric point (pI) below 5 or over 8. The peptide is expressed as a **fusion** protein (e.g., with a modified chloramphenicol acetyl transferase) in a host cell, and inclusion bodies containing the **fusion** protein are recovered. The **fusion** protein is cleaved under acidic conditions in the absence of a chaotrope, subsequently treated with a non-ionic chaotrope, and the desired peptide isolated by ion-exchange chromatography. The **fusion** partner protein has a C-terminal Asp - this Asp and the N-terminal amino acid of the desired peptide form a bond which can be cleaved under acid conditions. The **fusion** partner also promotes the formation of inclusion bodies with the host cell, and has a net charge sufficiently different from that of the peptide and any unwanted cleavage fragments to allow separation of the peptide by ion-exchange chromatography. The invention also encompasses a variation of the method of the invention whereby chaotrope-mediated solubilisation is replaced by the removal of insoluble cleavage products by ultrafiltration, diafiltration or centrifugation; an expression vector encoding the **fusion** protein; and a host cell containing the vector. The method of the invention is specifically used to produce b-type natriuretic peptide (BNP, pI>10) which is useful for treating congestive heart failure. This peptide improves heart function without direct cardiac stimulation, which may cause arrhythmia, and decreases levels of neurohormones which are associated with increased mortality and acceleration of disease progression. Cleavage of the **fusion** protein in the absence of a chaotrope results in a soluble peptide which is easily separated from the other (insoluble) cleavage products for subsequent purification. Sequences Z90228-Z90229 represent PCR primers used in an exemplification of the invention to modify DNA encoding the wild-type BNP protein to produce DNA encoding a truncated version of BNP wherein the initial serine of the mature BNP was absent. The N-terminal residue of the truncated BNP is Pro; in the modified chloramphenicol acetyl transferase (CAT)/truncated BNP **fusion** protein, the CAT portion is linked to the BNP portion via an Asp-**Pro peptide** bond. The presence of the Asp-Pro bond facilitates liberation of BNP as acid cleavage occurs most rapidly at an Asp-**Pro peptide** bond

L3 ANSWER 57 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000N-A10975 DNA DGENE

TITLE: Selective treatment of chronic pain by expressing beta-endorphin from a recombinant adenovirus vector in pia mater connective tissue cells, does not affect acute pain responses -

INVENTOR: Iadarola M J; Caudle R M; Finegold A A; Mannes A J

PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES

PATENT INFO: WO 2000016799 A1 20000330 39p

APPLICATION INFO: WO 1999-US21523 19990917

PRIORITY INFO: US 1998-100901 19980923

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-283447 [24]

AB This sequence represents a PCR primer used to amplify the mouse nerve growth factor (NGF) pre-**pro-sequence**. The pre-**pro-sequence** acts as a secretion signal for a beta-endorphin **fusion** protein used in the method of the invention. The invention relates to a method for treating chronic pain, by administering a recombinant adenovirus that expresses beta-endorphin into the subarachnoid space such that the basal nociceptive responses are not affected. The invention also relates to a pharmaceutical composition with analgesic activity, which contains the recombinant adenovirus. The method and pharmaceutical composition can be used to treat chronic pain. The treatment affects chronic pain selectively, with no significant effect on acute pain responses

L3 ANSWER 58 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000N-A10974 DNA DGENE

TITLE: Selective treatment of chronic pain by expressing beta-endorphin from a recombinant adenovirus vector in pia mater connective tissue cells, does not affect acute pain responses -

INVENTOR: Iadarola M J; Caudle R M; Finegold A A; Mannes A J

PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES

PATENT INFO: WO 2000016799 A1 20000330 39p

APPLICATION INFO: WO 1999-US21523 19990917

PRIORITY INFO: US 1998-100901 19980923

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-283447 [24]

AB This sequence represents a PCR primer used to amplify the mouse nerve growth factor (NGF) pre-**pro-sequence**. The pre-**pro-sequence** acts as a secretion signal for a beta-endorphin **fusion** protein used in the method of the invention. The invention relates to a method for treating chronic pain, by administering a recombinant adenovirus that expresses beta-endorphin into the subarachnoid space such that the basal nociceptive responses are not affected. The invention also relates to a pharmaceutical composition with analgesic activity, which contains the recombinant adenovirus. The method and pharmaceutical composition can be used to treat chronic pain. The treatment affects chronic pain selectively, with no significant effect on acute pain responses

L3 ANSWER 59 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1999N-V83967 DNA DGENE

TITLE: Preparation of recombinant polypeptides - by expression of a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen and a heterologous polypeptide

INVENTOR: Alcantara J; Moloney M; Van Rooijen G

PATENT ASSIGNEE: (SEMB-N)SEMBIOSYS GENETICS INC

PATENT INFO: WO 9849326 A1 19981105 44p

APPLICATION INFO: WO 1998-CA398 19980423

PRIORITY INFO: US 1997-44254 19970425

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1999-059646 [05]

AB The present sequence encodes a **fusion** protein comprising a His tag-bovine chymosin **pro-peptide**-carp growth hormone. The **fusion** protein was made to exemplify the invention. The specification describes a method for preparing a recombinant polypeptide in a host cell. A chimeric nucleic acid sequence encoding a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen linked a protein heterologous to the **pro-peptide**, is introduced into the host cell. The host cells are then grown to produce the **fusion** protein. Altering the environment of the **fusion** protein allows cleavage of the **pro-peptide** from the

fusion protein to release the recombinant polypeptide. The method can be used for the preparation of recombinant polypeptides such as hirudin or carp growth hormone. The **fusion** proteins can be used for delivering to a human or animal a therapeutic or nutritional polypeptide such as a vaccine, a peptide antibiotic, a cattle feed enzyme, a cytokine, a gastric lipase or a lactase

L3 ANSWER 60 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1999N-V83966 DNA DGENE
 TITLE: Preparation of recombinant polypeptides - by expression of a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen and a heterologous polypeptide
 INVENTOR: Alcantara J; Moloney M; Van Rooijen G
 PATENT ASSIGNEE: (SEMB-N)SEMBIOSYS GENETICS INC
 PATENT INFO: WO 9849326 A1 19981105 44p
 APPLICATION INFO: WO 1998-CA398 19980423
 PRIORITY INFO: US 1997-44254 19970425
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1999-059646 [05]

AB The present sequence encodes a **fusion** protein comprising glutathione-S-transferase (GST)-bovine chymosin **pro-peptide**-leech hirudin. The chymosin **pro-peptide** sequence is placed upstream of the DNA sequence encoding the leech anticoagulant protein hirudin. The **fusion** protein was made to exemplify the invention. The specification describes a method for preparing a recombinant polypeptide in a host cell. A chimeric nucleic acid sequence encoding a **fusion** protein comprising a **pro-peptide** derived from an autocatalytically maturing zymogen linked a protein heterologous to the **pro-peptide**, is introduced into the host cell. The host cells are then grown to produce the **fusion** protein. Altering the environment of the **fusion** protein allows cleavage of the **pro-peptide** from the **fusion** protein to release the recombinant polypeptide. The method can be used for the preparation of recombinant polypeptides such as hirudin or carp growth hormone. The **fusion** proteins can be used for delivering to a human or animal a therapeutic or nutritional polypeptide such as a vaccine, a peptide antibiotic, a cattle feed enzyme, a cytokine, a gastric lipase or a lactase

L3 ANSWER 61 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1998N-V11746 DNA DGENE
 TITLE: Recombinant yeast that secretes alpha-acetolactate decarboxylase - useful for making beer
 INVENTOR: Goelling D; Moench J; Stahl U
 PATENT ASSIGNEE: (BIOT-N)BIOTECN-GESES BIOTECHNOLOGISCHE
 PATENT INFO: DE 19641569 A1 19980416 12p
 APPLICATION INFO: DE 1996-19641569 19961009
 PRIORITY INFO: DE 1996-19641569 19961009
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 OTHER SOURCE: 1998-231485 [21]

AB PCR primers V11745 and V11746 are used in a method which results in the construction of a **fusion** protein composed of a pre-**pro** sequence from yeast alpha-factor (MF-alpha) fused to a yeast alpha-acetolactate decarboxylase (ALDC) protein fragment. This protein is used in the production of a novel type of brewers yeast. The yeast secretes ALDC into the brewing medium. The secreted ALDC converts alpha-acetolactate into acetoin, thus circumventing formation of diacetyl and reducing generation of an undesirable buttery taste in the beer

L3 ANSWER 62 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1998N-V11745 DNA DGENE
 TITLE: Recombinant yeast that secretes alpha-acetolactate decarboxylase - useful for making beer
 INVENTOR: Goelling D; Moench J; Stahl U
 PATENT ASSIGNEE: (BIOT-N)BIOTECN-GESES BIOTECHNOLOGISCHE
 PATENT INFO: DE 19641569 A1 19980416 12p
 APPLICATION INFO: DE 1996-19641569 19961009
 PRIORITY INFO: DE 1996-19641569 19961009
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 OTHER SOURCE: 1998-231485 [21]

AB PCR primers V11745 and V11746 are used in a method which results in the construction of a **fusion** protein composed of a pre-**pro** sequence from yeast alpha-factor (MF-alpha) fused to a yeast alpha-acetolactate decarboxylase (ALDC) protein fragment. This protein is

used in the production of a novel type of brewers yeast. The yeast secretes ALDC into the brewing medium. The secreted ALDC converts alpha-acetolactate into acetoin, thus circumventing formation of diacetyl and reducing generation of an undesirable buttery taste in the beer

L3 ANSWER 63 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998N-V44147 DNA DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor
 INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212
 PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 [30]

AB This sequence encodes a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human insulin-like growth factor, IGF-I-A as well as a human IGF propeptide. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 64 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998N-V44145 DNA DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor
 INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212
 PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 [30]

AB This sequence encodes a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human platelet derived growth factor type B (PDGF-B) and also contains a human propeptide sequence and an ADH/GAP promoter. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 65 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998N-V44137 DNA DGENE
 TITLE: Nucleotide sequence for expression of heterologous proteins in yeast - useful to produce heterologous mammalian proteins in biologically active, mature form, e.g. human platelet-derived growth factor
 INVENTOR: Merryweather J P; Tekamp-Olson P
 PATENT ASSIGNEE: (CHIR)CHIRON CORP
 PATENT INFO: WO 9826080 A1 19980618 81p
 APPLICATION INFO: WO 1997-US22647 19971212
 PRIORITY INFO: US 1996-32720 19961213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-348534 [30]

AB This sequence encodes a novel **fusion** protein constructed from the *Saccharomyces cerevisiae* alpha leader peptide and human platelet derived growth factor type B (PDGF-B) and also contains a human

propeptide sequence. This protein is used in a method which allows the expression of heterologous mammalian proteins and their secretion in the biologically active, mature form, by transforming yeast host cells with the vector and expressing the proteins. It is particularly useful to produce mammalian proteins whose assumption of a native conformation is facilitated by the presence of a native propeptide sequence in the precursor polypeptide. Expression and secretion of proteins in biologically active, mature form is possible, whilst previous methods have often encountered problems of post-translational processing leading to, e.g. production of inactive forms or insufficient amounts of protein

L3 ANSWER 66 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998N-V17947 DNA DGENE
 TITLE: New anti-atherosclerotic peptide(s) - have an amphipathic helical motif as the structural and functional domain and mimic human apoA-I
 INVENTOR: Anantharamaiah G M; Garber D W
 PATENT ASSIGNEE: (UABR-N)UAB RES FOUND
 PATENT INFO: WO 9809602 A2 19980312 41p
 APPLICATION INFO: WO 1997-US15721 19970905
 PRIORITY INFO: US 1996-25505 19960905
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1998-193304 [17]

AB The upper template used for producing the anti-atherosclerotic peptide gene contains a pre- and **pro-region** derived from the human apoA-I gene. Primer 18AU2 (V17948) was used to amplify the upper template in a PCR reaction which also contained the lower template (GMAL; V17949) of the peptide gene. As nucleotides 91-105 overlap with their corresponding sequence in the lower template, both templates are joined and amplified in the PCR reaction to form the complete peptide gene. The peptide gene encodes a DEP18A-P-18A peptide (W48634) where apart from the first 3 amino acids, the peptide is a head to tail dimer with a proline incorporation. Alternatively, the first three amino acids can be removed after expression to produce the 18A-P-18A peptide (W48633). The invention provides class A amphipathic helical peptides (18A; W48633, W48634 and W48635). The peptides had anti-atherosclerotic activity when tested in mice with diet induced atherosclerosis. Administration of the peptides also lowered total cholesterol levels in the mice. The peptides also mimicks many in vitro properties of human apolipoprotein A-I (apoA-I), e.g. they have a tandem repeating class A amphipathic helix linked by a proline which forms an optimal arrangement for lipid association, they have bilayer membrane stabilising properties and they also inhibit HIV-I gp41-induced cell **fusion**. Therefore these peptides can be used to inhibit and/or reverse atherosclerosis in animals

L3 ANSWER 67 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1997N-T68700 DNA DGENE
 TITLE: New active mutants of radish antifungal protein 2 - used to generate fungus-resistant plants or as therapeutic or preservative agents
 INVENTOR: Broekaert W F; De Samblanx G W; Rees S B
 PATENT ASSIGNEE: (ZENE)ZENECA LTD
 PATENT INFO: WO 9721814 A1 19970619 39p
 APPLICATION INFO: WO 1996-GB3065 19961212
 PRIORITY INFO: GB 1995-25474 19951213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1997-332785 [30]

AB Primer OWB62 (T68700) containing an NheI site was designed such that 7 extra nucleotides (coding for the last 2 amino acids of yeast mating factor alpha 1 **pro-sequence**) were added upstream of the coding region of mature radish antifungal protein 2 (Rs-AFP2) (see W19616). It was used with antisense primer OWB64 (T68699) in a second PCR amplification of the mature Rs-AFP2 coding sequence. Rs-AFP2 was subsequently expressed in yeast as a **fusion** protein with mating factor alpha 1. OWB61 was also used with antisense primer OWB36 (T68703) to amplify Rs-AFP2 mutant sequences. Mutants of Rs-AFP2 (see W26371-90) are claimed as novel salt tolerant antifungal proteins

L3 ANSWER 68 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1997N-T68698 DNA DGENE
 TITLE: New active mutants of radish antifungal protein 2 - used to generate fungus-resistant plants or as therapeutic or preservative agents
 INVENTOR: Broekaert W F; De Samblanx G W; Rees S B
 PATENT ASSIGNEE: (ZENE)ZENECA LTD
 PATENT INFO: WO 9721814 A1 19970619 39p
 APPLICATION INFO: WO 1996-GB3065 19961212

PRIORITY INFO: GB 1995-25474 19951213
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1997-332785 [30]

AB Primer OWB61 (T68698) containing an HindIII site was designed such that 16 extra nucleotides (coding for the last 5 amino acids of yeast mating factor alpha 1 **pro-sequence**) were added upstream of the coding region of mature radish antifungal protein 2 (Rs-AFP2) (see W19616). It was used with antisense primer OWB64 (T68699) in an initial PCR amplification of the mature Rs-AFP2 coding sequence. Rs-AFP2 was subsequently expressed in yeast as a **fusion** protein with mating factor alpha 1. OWB61 was also used with antisense primer OWB36 (T68703) to amplify Rs-AFP2 mutant sequences. Mutants of Rs-AFP2 (see W26371-90) are claimed as novel salt tolerant antifungal proteins

L3 ANSWER 69 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1996N-T27044 DNA DGENE
 TITLE: Recombinant human cathepsin O2 protein and related nucleic acid - useful as a collagenase in vitro and in vivo, e.g. in spinal disc problems and to dissolve the matrices around tumours
 INVENTOR: Broemme D; Okamoto K
 PATENT ASSIGNEE: (KHEP-N)KHEPRI PHARM INC
 PATENT INFO: WO 9613523 A1 19960509 82p
 APPLICATION INFO: WO 1995-US13820 19951026
 PRIORITY INFO: US 1995-536861 19951002
 US 1994-330121 19941027
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1996-239452 [24]

AB This primer may be used with primer T27043 to amplify a sequence encoding the **pro-region** of human prepro-cathepsin-O2. The **pro-region** may be expressed e.g. in plasmid pTrcHis as a histidine affinity tail **fusion** protein for subsequent purification and characterisation. Mature cathepsin-O2 has collagenase activity in vitro and in vivo, and may be used e.g. in therapy of spinal disc problems, pelvic or post-surgical adhesions, scars, keloids, cancer, endometriosis, pycnodysostosis or aberrant bone growth. The **pro-region** has cathepsin-O2-inhibitor activity, and may be used to treat cancer and bone disorders, or as a diagnostic agent. Antibodies against the full-length protein may be used diagnostically

L3 ANSWER 70 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1996N-T27043 DNA DGENE
 TITLE: Recombinant human cathepsin O2 protein and related nucleic acid - useful as a collagenase in vitro and in vivo, e.g. in spinal disc problems and to dissolve the matrices around tumours
 INVENTOR: Broemme D; Okamoto K
 PATENT ASSIGNEE: (KHEP-N)KHEPRI PHARM INC
 PATENT INFO: WO 9613523 A1 19960509 82p
 APPLICATION INFO: WO 1995-US13820 19951026
 PRIORITY INFO: US 1995-536861 19951002
 US 1994-330121 19941027
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1996-239452 [24]

AB This primer may be used with primer T27044 to amplify a sequence encoding the **pro-region** of human prepro-cathepsin-O2. The **pro-region** may be expressed e.g. in plasmid pTrcHis as a histidine affinity tail **fusion** protein for subsequent purification and characterisation. Mature cathepsin-O2 has collagenase activity in vitro and in vivo, and may be used e.g. in therapy of spinal disc problems, pelvic or post-surgical adhesions, scars, keloids, cancer, endometriosis, pycnodysostosis or aberrant bone growth. The **pro-region** has cathepsin-O2-inhibitor activity, and may be used to treat cancer and bone disorders, or as a diagnostic agent. Antibodies against the full-length protein may be used diagnostically

L3 ANSWER 71 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1996N-T13792 DNA DGENE
 TITLE: Prod'n. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein
 INVENTOR: Hastrup S; Fabricius W O E L D I K E
 PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS
 PATENT INFO: WO 9617943 A1 19960613 41p

APPLICATION INFO: WO 1995-DK498 19951208
PRIORITY INFO: DK 1994-1411 19941209
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus* serine proteases, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Two primers (T13791, T13792) were used to amplify the prepro-part of the *Bacillus subtilis* savinase gene (Subtilisin 309) for its **fusion** to the mature *Humicola insolens* lipase

L3 ANSWER 72 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1996N-T13791 DNA DGENE
TITLE: Prodn. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein
INVENTOR: Hastrup S; Fabricius W O E L D I K E
PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS
PATENT INFO: WO 9617943 A1 19960613 41p
APPLICATION INFO: WO 1995-DK498 19951208
PRIORITY INFO: DK 1994-1411 19941209
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus* serine proteases, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Two primers (T13791, T13792) were used to amplify the prepro-part of the *Bacillus subtilis* savinase gene (Subtilisin 309) for its **fusion** to the mature *Humicola insolens* lipase

L3 ANSWER 73 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1996N-T13790 DNA DGENE
TITLE: Prodn. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein
INVENTOR: Hastrup S; Fabricius W O E L D I K E
PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS
PATENT INFO: WO 9617943 A1 19960613 41p
APPLICATION INFO: WO 1995-DK498 19951208
PRIORITY INFO: DK 1994-1411 19941209
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus* serine proteases, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Four primers (T13787-90) were used to produce an *Achromobacter lyticus* protease I/*Humicola insolens* lipase **fusion**

L3 ANSWER 74 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1996N-T13789 DNA DGENE
TITLE: Prodn. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein
INVENTOR: Hastrup S; Fabricius W O E L D I K E
PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS

PATENT INFO: WO 9617943 A1 19960613 41p
 APPLICATION INFO: WO 1995-DK498 19951208
 PRIORITY INFO: DK 1994-1411 19941209
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus serine proteases*, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Four primers (T13787-90) were used to produce an *Achromobacter lyticus* protease I/*Humicola insolens* lipase **fusion**

L3 ANSWER 75 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1996N-T13788 DNA DGENE

TITLE: Prodn. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein

INVENTOR: Hastrup S; Fabricius W O E L D I K E

PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS

PATENT INFO: WO 9617943 A1 19960613 41p

APPLICATION INFO: WO 1995-DK498 19951208

PRIORITY INFO: DK 1994-1411 19941209

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus serine proteases*, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Four primers (T13787-90) were used to produce an *Achromobacter lyticus* protease I/*Humicola insolens* lipase **fusion**

L3 ANSWER 76 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1996N-T13787 DNA DGENE

TITLE: Prodn. of extracellular proteins in bacteria with inner and outer cell membranes - using vector contg. DNA construct encoding pre:**pro:peptide** of bacterial extracellular protease operably connected to DNA encoding target protein

INVENTOR: Hastrup S; Fabricius W O E L D I K E

PATENT ASSIGNEE: (NOVO)NOVO-NORDISK AS

PATENT INFO: WO 9617943 A1 19960613 41p

APPLICATION INFO: WO 1995-DK498 19951208

PRIORITY INFO: DK 1994-1411 19941209

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1996-287187 [29]

AB Recombinant production of an extracellular protein in a bacterium provided with both an inner and outer cell membrane is achieved by producing a vector construct comprising the prepropeptide or part of the prepropeptide of a bacterial extracellular protease selected from *Achromobacter lyticus* protease I, *Bacillus metalloproteases* and *Bacillus serine proteases*, operably linked to the sequence encoding the desired protein. This vector construct is then used to transform the bacterium which is then cultured. The desired protein is then harvested from the culture medium. Four primers (T13787-90) were used to produce an *Achromobacter lyticus* protease I/*Humicola insolens* lipase **fusion**

L3 ANSWER 77 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q92062 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC

PATENT INFO: US 5411873 A 19950502 32p

APPLICATION INFO: US 1984-614612 19840529

PRIORITY INFO: US 1986-846627 19860401

US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB The sequence of a primer used to create the plasmid pPA390 containing the first 45 codons of the human growth hormone sequence linked to codons 45-100 of preprosubtilisin (see Q90041). The plasmid also includes the Pac promoter and ribosome binding site, the amylase signal sequence and 32 codons of the mature amylase sequence. The plasmid is used to produce a human growth hormone-subtilisin **fusion** protein. This is an example of a use for a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein e.g. the human growth hormone (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 78 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q92061 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC

PATENT INFO: US 5411873 A 19950502 32p

APPLICATION INFO: US 1984-614612 19840529

PRIORITY INFO: US 1986-846627 19860401

US 1984-614612 19840529

US 1990-488433 19900227

US 1992-928697 19920811

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1995-178127 [23]

AB Oligonucleotides Q90044-5 and Q92059-62 were used to produce a series of mutated subtilisin genes from Bacillus amyloliquefaciens (Q90041) by site-directed mutagenesis. The mutated genes encode subtilisin proteins that are incapable of autoproteolytic maturation. This primer changes the protein sequence at pos. 48 from Ala to Arg. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 79 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q92060 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC

PATENT INFO: US 5411873 A 19950502 32p

APPLICATION INFO: US 1984-614612 19840529

PRIORITY INFO: US 1986-846627 19860401

US 1984-614612 19840529

US 1990-488433 19900227

US 1992-928697 19920811

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1995-178127 [23]

AB Oligonucleotides Q90044-5 and Q92059-61 were used to produce a series of mutated subtilisin genes from Bacillus amyloliquefaciens (Q90041) by site-directed mutagenesis. The mutated genes encode subtilisin proteins that are incapable of autoproteolytic maturation. This primer creates an in-frame deletion of codon -102 to -98 in the subtilisin signal sequence. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 80 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q92059 DNA DGENE
TITLE: Recovery of recombinant subtilisin mutants from host cells -
by treatment with active subtilisin to cleave mutant from its
pro-sequence
INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB Oligonucleotides Q90044-5 and Q92059-62 were used to produce a series of mutated subtilisin genes from *Bacillus amyloliquefaciens* (Q90041) by site-directed mutagenesis. The mutated genes encode subtilisin proteins that are incapable of autoproteolytic maturation. This primer creates a 7 bp deletion and a frameshift starting at codon 163. The frameshift causes premature chain termination 21 codons further downstream, resulting in a truncated protein. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B.subtilis* subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 81 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995N-Q90045 DNA DGENE
TITLE: Recovery of recombinant subtilisin mutants from host cells -
by treatment with active subtilisin to cleave mutant from its
pro-sequence
INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB Oligonucleotides Q90044-5 and Q92059-62 were used to produce a series of mutated subtilisin genes from *Bacillus amyloliquefaciens* (Q90041) by site-directed mutagenesis. The mutated genes encode subtilisin proteins that are incapable of autoproteolytic maturation. This primer changes the protein sequence at pos. 32 from Asp to Asn. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B.subtilis* subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 82 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995N-Q90044 DNA DGENE
TITLE: Recovery of recombinant subtilisin mutants from host cells -
by treatment with active subtilisin to cleave mutant from its
pro-sequence
INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G
PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB Oligonucleotides Q90044-5 and Q92059-62 were used to produce a series of mutated subtilisin genes from *Bacillus amyloliquefaciens* (Q90041) by site-directed mutagenesis. The mutated genes encode subtilisin proteins that are incapable of autoproteolytic maturation. This primer, corresponding to the sequence encoding amino acids 216-232, creates a

loss of the sequence encoding amino acids 222-225 and alters to the sequence for amino acids 220, 227 and 228 to create a KpnI restriction enzyme site. An oligonucleotide is inserted into this site which corresponds to the sequence encoding the wild type amino acids 222-228 and causes an alteration at pos. 221 from a Ser residue to an Ala residue. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin (Q90042) or neutral protease (Q90043)

L3 ANSWER 83 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q90043 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC

PATENT INFO: US 5411873 A 19950502 32p

APPLICATION INFO: US 1984-614612 19840529

PRIORITY INFO: US 1986-846627 19860401

US 1984-614612 19840529

US 1990-488433 19900227

US 1992-928697 19920811

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1995-178127 [23]

AB The nucleotide sequence of the Bacillus subtilis neutral protease gene. The gene is used in a method to produce a carbonyl hydrolase (subtilisin) e.g. the B.amyloliquefaciens subtilisin (Q90041) or other heterologous protein e.g. human growth hormone (produced as a **fusion** protein), such that the desired protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The B.amyloliquefaciens sequence was mutated using the primers Q90044-5 and Q*****-, specifically at S221N, D32N, A48R or contained a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 84 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q90042 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC

PATENT INFO: US 5411873 A 19950502 32p

APPLICATION INFO: US 1984-614612 19840529

PRIORITY INFO: US 1986-846627 19860401

US 1984-614612 19840529

US 1990-488433 19900227

US 1992-928697 19920811

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1995-178127 [23]

AB The nucleotide sequence of the Bacillus subtilis subtilisin gene. The gene is used in a method to produce a carbonyl hydrolase (subtilisin) e.g. the B.amyloliquefaciens subtilisin (Q90041) or other heterologous protein (produced as a **fusion** protein) e.g. human growth hormone, such that the desired protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. B.subtilis subtilisin or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The B.amyloliquefaciens sequence was mutated using the primers Q90044-5 and Q*****-, specifically at S221N, D32N, A48R or contained a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 85 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q90041 DNA DGENE

TITLE: Recovery of recombinant subtilisin mutants from host cells - by treatment with active subtilisin to cleave mutant from its **pro-sequence**

INVENTOR: Adams R M; Power S D; Powers D B; Wells J A; Yansura D G

PATENT ASSIGNEE: (GEMV)GENENCOR INC
PATENT INFO: US 5411873 A 19950502 32p
APPLICATION INFO: US 1984-614612 19840529
PRIORITY INFO: US 1986-846627 19860401
US 1984-614612 19840529
US 1990-488433 19900227
US 1992-928697 19920811

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-178127 [23]

AB The nucleotide sequence of the *Bacillus amyloliquefaciens* subtilisin gene. The gene is mutated in a method to produce a carbonyl hydrolase (subtilisin) or other heterologous protein (produced as a **fusion** protein) such that the protein is translated as a preproprotein which can be transported across the cell membrane but is not released as an enzymatically functional protein until the application of an external protease or a protease encoded by the host cell e.g. *B. subtilis* subtilisin (Q90042) or neutral protease (Q90043). The preproprotein sequence is mutated so that it is incapable of autoproteolytic maturation. The *B. amyloliquefaciens* sequence was mutated using the primers Q90044-5 and Q*****, specifically at S221N, D32N, A48R or a deletion of 166 amino acids from the C-terminus of the protein

L3 ANSWER 86 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q83668 DNA DGENE
TITLE: Secretion sequence for prodn. of a heterologous protein in yeast - useful for the expression of insulin-like growth factor-1

INVENTOR: Brierley R A; Howland D S; Scott R W
PATENT ASSIGNEE: (CEPH-N)CEPHALON INC
PATENT INFO: WO 9507978 A 19950323 80p
APPLICATION INFO: WO 1994-US9653 19940824
PRIORITY INFO: US 1993-122889 19930916
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-131346 [17]

AB PKD is a template DNA (partial sequence shown here) for a **fusion** gene contg. the coding sequences for human insulin-like growth factor-I (IGF-I) and peptide sequences necessary for secretion of the protein, ie. the PHO signal peptide, which in PSS and all other recombinant templates contg. the acid phosphatase signal sequence, an L to F substitution at amino acid 6 of the signal peptide was made by changing codon CTA (present in native PHO sequence) to TCC. The recombinant DNA is used to express a protein in yeast cells. The signal peptide ensures secretion of the heterologous protein which can then be isolated from the yeast cell culture supernatant. The DNA sequence can also be used to determine the ability of a secretory facilitating element, ie. the *K. lactis* **pro sequence** as in this template, or signal peptide to direct secretion of a protein from a yeast host. The element is inserted into the DNA and can be assayed (see also Q83665-74)

L3 ANSWER 87 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q83667 DNA DGENE
TITLE: Secretion sequence for prodn. of a heterologous protein in yeast - useful for the expression of insulin-like growth factor-1

INVENTOR: Brierley R A; Howland D S; Scott R W
PATENT ASSIGNEE: (CEPH-N)CEPHALON INC
PATENT INFO: WO 9507978 A 19950323 80p
APPLICATION INFO: WO 1994-US9653 19940824
PRIORITY INFO: US 1993-122889 19930916
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-131346 [17]

AB PKV is a template DNA (partial sequence shown here) for a **fusion** gene contg. the coding sequences for human insulin-like growth factor-I (IGF-I) and peptide sequences necessary for secretion of the protein, ie. the PHO signal peptide, which in PSS and all other recombinant templates contg. the acid phosphatase signal sequence, an L to F substitution at amino acid 6 of the signal peptide was made by changing codon CTA (present in native PHO sequence) to TCC. The recombinant DNA is used to express a protein in yeast cells. The signal peptide ensures secretion of the heterologous protein which can then be isolated from the yeast cell culture supernatant. The DNA sequence can also be used to determine the ability of a secretory facilitating element, ie. the *K. lactis* **pro sequence** as in this template, or signal peptide to direct secretion of a protein from a yeast host. The element is inserted into the DNA and can be assayed (see also Q83665-74)

L3 ANSWER 88 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q83195 DNA DGENE
TITLE: Modified Yarrowia lipolytica LEU2 gene promoters and genes -
also expression vectors contg them for multiple integration
into Y lipolytica to express and secrete heterologous protein
INVENTOR: James L C; Strick C A
PATENT ASSIGNEE: (PFIZ)PFIZER INC
PATENT INFO: WO 9506739 A 19950309 57p
APPLICATION INFO: WO 1994-IB128 19940530
PRIORITY INFO: US 1993-117375 19930902
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-115454 [15]
AB The proinsulin analogue (A14trp) coding sequence was ligated to a vector
(pXPRUAcas) contg. XPR2 promotor, pre- and pro-sequences followed by a
multiple cloning site and XPR2 terminator sequences along with a
wild-type URA3 gene as selectable marker. The ligation created an
in-frame **fusion** between the last codon of the Y. lipolytica
XPR2 **pro region** and the first codon of proinsulin
analogue A14trp. Modified promoters, from Y. lipolytica can be used to
express heterologous proteins, esp. A14Trp proinsulin and insulinotropin

L3 ANSWER 89 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q75454 DNA DGENE
TITLE: New **fusion** polypeptide(s) and glycosylation
inhibition factor - used to develop prods. for suppressing an
undesirable response, partic. allergies and auto:immune
disease
INVENTOR: Ishizaka K; Liu Y; Mikayama T
PATENT ASSIGNEE: (KIRI)KIRIN BEER KK
(LJOL-N) LA JOLLA INST ALLERGY & IMMUNOLOGY
PATENT INFO: WO 9426923 A 19941124 156p
APPLICATION INFO: WO 1994-US5354 19940513
PRIORITY INFO: US 1993-61041 19930514
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-006814 [01]
AB The cDNA fragment encoding the signal peptide and N-terminal **pro**
-region of human pro-calcitonin (pro-CT) was amplified by PCR
using human calcitonin cDNA as template. mRNA was isolated from human
thyroid carcinoma TT cells and reverse transcribed into cDNA which was
used as the PCR template. Oligo primers having a PstI site (Q75453 and
Q75454) were synthesised and the human calcitonin precursor gene was
amplified

L3 ANSWER 90 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-Q75453 DNA DGENE
TITLE: New **fusion** polypeptide(s) and glycosylation
inhibition factor - used to develop prods. for suppressing an
undesirable response, partic. allergies and auto:immune
disease
INVENTOR: Ishizaka K; Liu Y; Mikayama T
PATENT ASSIGNEE: (KIRI)KIRIN BEER KK
(LJOL-N) LA JOLLA INST ALLERGY & IMMUNOLOGY
PATENT INFO: WO 9426923 A 19941124 156p
APPLICATION INFO: WO 1994-US5354 19940513
PRIORITY INFO: US 1993-61041 19930514
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-006814 [01]
AB The cDNA fragment encoding the signal peptide and N-terminal **pro**
-region of human pro-calcitonin (pro-CT) was amplified by PCR
using human calcitonin cDNA as template. mRNA was isolated from human
thyroid carcinoma TT cells and reverse transcribed into cDNA which was
used as the PCR template. Oligo primers having a PstI site (Q75453 and
Q75454) were synthesised and the human calcitonin precursor gene was
amplified

L3 ANSWER 91 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-T09054 DNA DGENE
TITLE: **Fusion** gene coding for albumin fused to human
apo:lipoprotein E - also vectors and transformed yeast for
prepn. of **fusion** protein as intermediate for drugs,
reagents and apo:lipoprotein E
PATENT ASSIGNEE: (BEPP-I)BEPPU T
PATENT INFO: JP 07241196 A 19950919 12p
APPLICATION INFO: JP 1994-58270 19940304
PRIORITY INFO: JP 1994-58270 19940304
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: 1995-354277 [46]

AB Primers T09051-63 are used to produce a novel **fusion** protein consisting of the human albumin linked N-terminally to the human apolipoprotein E. The primers T09053-4 were used to remove the human albumin gene **pro-sequence**. The resultant fragment was cloned into the plasmid pUC19 to produce plasmid pALB2. The **fusion** gene is cloned into a yeast plasmid and expressed in *S.cerevisiae*. The **fusion** protein is useful as an intermediate for the synthesis of reagents, drugs and apolipoprotein E-like proteins

L3 ANSWER 92 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995N-T09053 DNA DGENE

TITLE: **Fusion** gene coding for albumin fused to human apo:lipoprotein E - also vectors and transformed yeast for prepn. of **fusion** protein as intermediate for drugs, reagents and apo:lipoprotein E

PATENT ASSIGNEE: (BEPP-I)BEPPU T

PATENT INFO: JP 07241196 A 19950919 12p

APPLICATION INFO: JP 1994-58270 19940304

PRIORITY INFO: JP 1994-58270 19940304

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: 1995-354277 [46]

AB Primers T09051-63 are used to produce a novel **fusion** protein consisting of the human albumin linked N-terminally to the human apolipoprotein E. The primers T09053-4 were used to remove the human albumin gene **pro-sequence**. The resultant fragment was cloned into the plasmid pUC19 to produce plasmid pALB2. The **fusion** gene is cloned into a yeast plasmid and expressed in *S.cerevisiae*. The **fusion** protein is useful as an intermediate for the synthesis of reagents, drugs and apolipoprotein E-like proteins

L3 ANSWER 93 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994N-Q71558 DNA DGENE

TITLE: New multimeric polypeptide comprising fused subunits of natural protein. - and related DNA and transformed cells, esp. dimers of platelet derived growth factor, useful for stimulating healing of wounds

INVENTOR: Thomason A R

PATENT ASSIGNEE: (AMGE-N)AMGEN INC

PATENT INFO: EP 618227 A 19941005 30p

APPLICATION INFO: EP 1994-105075 19940331

PRIORITY INFO: US 1993-41635 19930401

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-304405 [38]

AB The PDGF-B 109 subunit coding sequence was obtained as composite sequence of fragments from human PDGF-B pre-**pro region**, human v-sis gene and synthetic fragments. The mature 109 amino acid subunit was incorporated into a single polypeptide with a PDGF-B 119 subunit, pref. separated by a peptide linker to produce a preferred **fusion** polypeptide of the invention. The **fusion** polypeptide is useful for treating wounds

L3 ANSWER 94 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994N-Q70104 cDNA DGENE

TITLE: New nucleic acid encoding enterokinase activity - and related vectors, host cells, expression products and antibodies are useful in treating digestive disorders and for cleaving **fusion** proteins

INVENTOR: Lavallie E R

PATENT ASSIGNEE: (GEMY)GENETICS INST INC

PATENT INFO: WO 9416083 A 19940721 50p

APPLICATION INFO: WO 1994-US616 19940113

PRIORITY INFO: US 1993-5944 19930115

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-249229 [30]

AB The enterokinase (EK) (or the EK gene when used in gene therapy) is used to treat digestive disorders associated with low EK activity (esp. inability to process trypsinogen to trypsin). For cleaving **fusion** proteins, recombinant EK catalytic domain is much more efficient than the native two-chain holoenzyme and is not contaminated by other proteolytic enzymes. For expression of recombinant EK, the 1691-2398 DNA fragment was fused to the 3'-end of the signal peptide and **pro-region** of the human PACE gene. The prod. could be expressed in CHO cells to produce a chimaeric prod. from which the **pro-region** as cleaved by endogenous PACE, providing

mature EK catalytic domain

L3 ANSWER 95 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994N-Q68595 DNA DGENE

TITLE: Eukaryotic cutinase variants with improved lipolytic activity
- with modified amino acid structure to improve compatibility
with anionic surfactantsINVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
T W M; Verrips C TPATENT ASSIGNEE: (UNIL)UNILEVER NV
(UNIL) UNILEVER PLC

PATENT INFO: WO 9414964 A 19940707 72p

APPLICATION INFO: WO 1993-EP3551 19931209

PRIORITY INFO: EP 1992-204079 19921223

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* exlA. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the exlA pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the exlA pre- sequence is fused with the N-terminal residue of mature cutinase. Cassette 7 is identical with cassette 6, but here the N-terminal residue of the encoded mature cutinase polypeptide has been changed from the original G to S in order to better fit the requirements for cleavage of the signal peptide. Cassettes 5,6 and 7 were assembled from the synthetic oligos

L3 ANSWER 96 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994N-Q68594 DNA DGENE

TITLE: Eukaryotic cutinase variants with improved lipolytic activity
- with modified amino acid structure to improve compatibility
with anionic surfactantsINVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
T W M; Verrips C TPATENT ASSIGNEE: (UNIL)UNILEVER NV
(UNIL) UNILEVER PLC

PATENT INFO: WO 9414964 A 19940707 72p

APPLICATION INFO: WO 1993-EP3551 19931209

PRIORITY INFO: EP 1992-204079 19921223

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* exlA. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the exlA pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the exlA pre- sequence is fused with the N-terminal residue of mature cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 97 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1994N-Q68593 DNA DGENE

TITLE: Eukaryotic cutinase variants with improved lipolytic activity
- with modified amino acid structure to improve compatibility
with anionic surfactantsINVENTOR: De Vlieg J; Egmond M R; Musters W; Peters H; Van Der Hijden H
T W M; Verrips C TPATENT ASSIGNEE: (UNIL)UNILEVER NV
(UNIL) UNILEVER PLC

PATENT INFO: WO 9414964 A 19940707 72p

APPLICATION INFO: WO 1993-EP3551 19931209

PRIORITY INFO: EP 1992-204079 19921223

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1994-234699 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* exlA. To prepare the synthetic cutinase gene for

such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the ex1A pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 5 this connection is made by fusing the ex1A pre-sequence to the **pro-sequence** of cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 98 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994N-Q68587 DNA DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Van D E R ;
 Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* ex1A. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the ex1A pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the ex1A pre- -sequence is fused with the N-terminal residue of mature cutinase. Cassette 7 is identical with cassette 6, but here the N-terminal residue of the encoded mature cutinase polypeptide has been changed from the original G to S in order to better fit the requirements for cleavage of the signal peptide. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 99 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994N-Q68586 DNA DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Van D E R ;
 Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* ex1A. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the ex1A pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 6 the ex1A pre- -sequence is fused with the N-terminal residue of mature cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 100 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994N-Q68585 DNA DGENE
 TITLE: Eukaryotic cutinase variants with improved lipolytic activity
 - useful in detergent compsns., with modified amino acid
 compsn. to increase hydrophobicity
 INVENTOR: De V L I E G ; Egmond M R; Musters W; Peters H; Van D E R ;
 Verrips C T
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9414963 A 19940707 77p
 APPLICATION INFO: WO 1993-EP3550 19931209
 PRIORITY INFO: EP 1992-204025 19921218
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-234698 [28]

AB For the expression of a synthetic *Fusarium solani* pisi cutinase gene in *Aspergillus niger* var. *awamori*, expression vectors were constructed in which a synthetic gene encoding the mature cutinase is not preceded by its own pre-**pro-sequence**, but by the pre-sequence of *A. niger* var. *awamori* *exlA*. To prepare the synthetic cutinase gene for such **fusion**, several adaptor fragments were synthesised in which the coding sequence for the *exlA* pre-sequence is connected to the sequence encoding the N-terminus of mature cutinase in different ways. In cassette 5 this connection is made by fusing the *exlA* pre-sequence to the **pro-sequence** of cutinase. Cassettes 5, 6 and 7 were assembled from synthetic oligos

L3 ANSWER 101 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1994N-Q57029 DNA DGENE
 TITLE: Enzyme-contg. detergent compsns. - comprises anionic-nonionic surfactant system, and a lipolytic enzyme pref. a fungal cutinase derived from *F. solani* pisi
 INVENTOR: Hondmann D H A; Klugkist J; Marugg J D; Musters W; Van der Hijden H T W M; Warr J F
 PATENT ASSIGNEE: (UNIL)UNILEVER NV
 (UNIL) UNILEVER PLC
 PATENT INFO: WO 9403578 A 19940217 67p
 APPLICATION INFO: WO 1993-EP1923 19930720
 PRIORITY INFO: GB 1992-16387 19920731
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1994-065669 [08]

AB This sequence represents cassette 5 and was used in the expression of the *Fusarium solani* pisi cutinase gene in *Aspergillus niger*. This sequence contains the *A. niger* strong inducible *exlA* promoter and the cutinase **pro-sequence** N-terminal. The *F. solani* pisi cutinase gene was used in the production of the cutinase enzyme for use in an enzymatic detergent composition. The composition also comprises (by wt.) 0.1-50% of a surfactant system comprising 0-95% of 1 or more anionic surfactants and 5-100% of 1 or more nonionic surfactants. The composition exhibits a substantial lipolytic activity during the main cycle of a wash process in an automatic washing machine, and consequently produces lipolytic activity when used to wash fabrics which have not been in contact with the detergent product before. The composition is also especially suitable for use in combination with a tumble drier

L3 ANSWER 102 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1993N-Q49929 DNA DGENE
 TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**
 INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
 PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
 PATENT INFO: WO 9320214 A 19931014 30p
 APPLICATION INFO: WO 1993-US3018 19930330
 PRIORITY INFO: US 1992-860468 19920330
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 103 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1993N-Q49928 DNA DGENE
 TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**
 INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
 PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
 PATENT INFO: WO 9320214 A 19931014 30p
 APPLICATION INFO: WO 1993-US3018 19930330
 PRIORITY INFO: US 1992-860468 19920330
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the

construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 104 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49927 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 105 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49926 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 106 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49925 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction

between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 107 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49924 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 108 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49923 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 109 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49922 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 110 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49921 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus

pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 111 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49920 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. *bacillus*

pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 112 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49919 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. *bacillus*

pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 113 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49918 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. *bacillus*

pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 114 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49917 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 115 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49916 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 116 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49915 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the

chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 117 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49914 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 118 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49913 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 119 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49912 DNA DGENE

TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A

PATENT ASSIGNEE: (GEMV)GENENCOR INT INC

PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330

PRIORITY INFO: US 1992-860468 19920330

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of Pseudomonas mendocina ATCC 53552 lipase (cutinase) in Bacillus. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a Bacillus gene. The plasmids were then integrated into the chromosome of a Bacillus production host and a mutation, pref. sacU(Hy), introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 120 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993N-Q49911 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids
containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 121 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993N-Q49910 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids
containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 122 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993N-Q49909 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids
containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, pref. *sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 123 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993N-Q49908 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids
containing lipase unfused or fused to e.g. bacillus
pro-sequence

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p

APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, *pref. sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 124 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993N-Q49907 DNA DGENE
TITLE: Process for expressing lipase protein - using plasmids containing lipase unfused or fused to e.g. *bacillus* **pro-sequence**

INVENTOR: Carlomagno L P; Power S D; Van Kimmenade J M A
PATENT ASSIGNEE: (GEMV)GENENCOR INT INC
PATENT INFO: WO 9320214 A 19931014 30p
APPLICATION INFO: WO 1993-US3018 19930330
PRIORITY INFO: US 1992-860468 19920330
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-336921 [42]

AB The sequences given in Q49907-29 are primers which were used in the construction of a series of plasmids for the expression of *Pseudomonas mendocina* ATCC 53552 lipase (cutinase) in *Bacillus*. The plasmids contained the mature lipase gene fused to one of the first to ninth amino acids of a *Bacillus* gene. The plasmids were then integrated into the chromosome of a *Bacillus* production host and a mutation, *pref. sacU(Hy)*, introduced in to this construct by PCR. This method may be used to optimise heterologous secretion by changing the **fusion** junction between the donor gene and the target mature gene. This may be used to express large amounts of lipase

L3 ANSWER 125 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993N-Q42571 DNA DGENE
TITLE: Eukaryotic expression of neurotrophins - using prepro region of a different neurotrophin for more efficient post-translational processing

INVENTOR: Gies D; Hu S S; Ip N; Squinto S P; Yancopoulos G D
PATENT ASSIGNEE: (AMGE-N)AMGEN
(REGE-N) REGENERON PHARM INC
PATENT INFO: WO 9310150 A 19930527 80p
APPLICATION INFO: WO 1992-US9792 19921113
PRIORITY INFO: US 1991-792492 19911114
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1993-182492 [22]

AB This sequence encodes nerve growth factor (NGF). The protein encoded by this sequence promotes the development of the peripheral nervous system and also influences the development and maintenance of specific populations of neurons in the central nervous system. Two major transcripts from the NGF gene result in a "long" and "short" NGF prepropeptide. The "short" precursor contains a conventional signal sequence at the N-terminus which flanks the **pro-region**. The "long" precursor contains an additional **pro-region** at its N-terminal. No functional distinction has been elucidated between the "long" and "short" forms. Characteristics of NGF, such as isoelectric point and primary structure, are very similar to brain derived neurotrophic factor (BDNF). The NGF coding sequence may be used in the construction of a chimeric nucleic acid molecule to encode a prepro- NGF/BDNF chimera (see also Q42568-69)

L3 ANSWER 126 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992N-Q27469 DNA DGENE
TITLE: DNA fragment for prodn. of human serum albumin - comprises expression cassette including promoter and terminator sequences of methanol responsive gene, for expression in methylotrophic yeast

INVENTOR: Davis G R; Provow S A
PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNOLOGY IND ASSOC
PATENT INFO: WO 9213951 A 19920820 75p
APPLICATION INFO: WO 1992-US1015 19920204

PRIORITY INFO: US 1991-650040 19910204
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-300037 [36]

AB The sequences given in Q27468-9 are probes which were used in the isolation of a synthetic HSA gene and in the construction of the expression cassette of the invention in plasmid pHSA111. pHSA111 is identical to plasmid pHSA211 (see Q27465-7) except that pHSA111 contains the native 24-amino acid HSA secretion signal (see Q27464) instead of the alpha-mating factor (AMF) pre-**pro sequence** (see Q27463). The signal sequence was designed using yeast preferred codons to place an EcoRI site immediately 5' of the initiation codon and to delete the codon for methionine from the 5' end of the HSA gene in the vector pMET-HSA. The signal sequence and HSA gene were cloned into plasmid pHSA105 and sequenced. The **fusion** sequence was then cloned into the Pichia pastoris vector pAO856. This resulted in the production of an expression cassette comprising the HSA structural gene and signal sequence under the control of the P. pastoris AOX1 promoter and regulatory regions, as well as the AOX1 transcription termination and polyadenylation signals

L3 ANSWER 127 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q27468 DNA DGENE
TITLE: DNA fragment for prodn. of human serum albumin - comprises expression cassette including promoter and terminator sequences of methanol responsive gene, for expression in methylotrophic yeast
INVENTOR: Davis G R; Provow S A
PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNOLOGY IND ASSOC
PATENT INFO: WO 9213951 A 19920820 75p
APPLICATION INFO: WO 1992-US1015 19920204
PRIORITY INFO: US 1991-650040 19910204
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-300037 [36]

AB The sequences given in Q27468-9 are probes which were used in the isolation of a synthetic HSA gene and in the construction of the expression cassette of the invention in plasmid pHSA111. pHSA111 is identical to plasmid pHSA211 (see Q27465-7) except that pHSA111 contains the native 24-amino acid HSA secretion signal (see Q27464) instead of the alpha-mating factor (AMF) pre-**pro sequence** (see Q27463). The signal sequence was designed using yeast preferred codons to place an EcoRI site immediately 5' of the initiation codon and to delete the codon for methionine from the 5' end of the HSA gene in the vector pMET-HSA. The signal sequence and HSA gene were cloned into plasmid pHSA105 and sequenced. The **fusion** sequence was then cloned into the Pichia pastoris vector pAO856. This resulted in the production of an expression cassette comprising the HSA structural gene and signal sequence under the control of the P. pastoris AOX1 promoter and regulatory regions, as well as the AOX1 transcription termination and polyadenylation signals

L3 ANSWER 128 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q27467 DNA DGENE
TITLE: DNA fragment for prodn. of human serum albumin - comprises expression cassette including promoter and terminator sequences of methanol responsive gene, for expression in methylotrophic yeast
INVENTOR: Davis G R; Provow S A
PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNOLOGY IND ASSOC
PATENT INFO: WO 9213951 A 19920820 75p
APPLICATION INFO: WO 1992-US1015 19920204
PRIORITY INFO: US 1991-650040 19910204
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-300037 [36]

AB The sequences given in Q27465-7 are probes which were used in the isolation of a synthetic HSA gene and in the construction of the expression cassette of the invention in plasmid pHSA211. The HSA gene (see Q27462) was cloned in the plasmid pMET-HSA. Mutagenising oligonucleotides were used to introduce and delete restriction sites to facilitate further cloning. The HSA gene was then cloned into plasmid M13mp10 to give vector pHSA101. A termination codon was introduced to the 3' of the HSA gene. The HSA gene was then cloned into plasmid pAO203, which is a plasmid containing the alpha-mating factor (AMF) pre-**pro sequence** (see Q27463). The resulting plasmid contained DNA encoding the 83-amino acid leader sequence of the AMF pre-**pro region** followed by the processing sites, Lys-Arg and (Glu-Ala)₂, joined to the DNA encoding the HSA gene. The (Glu-Ala)₂

processing site was then deleted and the pre-pro AMF-HSA **fusion** was then cloned into the Pichia pastoris vector pAO856. This resulted in the production of an expression cassette encoding the pre-pro AMF-HSA **fusion** gene under the control of the P. pastoris AOX1 promoter and regulatory regions, as well as the AOX1 transcription termination and polyadenylation signals

L3 ANSWER 129 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q27466 DNA DGENE
 TITLE: DNA fragment for prodn. of human serum albumin - comprises expression cassette including promoter and terminator sequences of methanol responsive gene, for expression in methylotrophic yeast
 INVENTOR: Davis G R; Provow S A
 PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNOLOGY IND ASSOC
 PATENT INFO: WO 9213951 A 19920820 75p
 APPLICATION INFO: WO 1992-US1015 19920204
 PRIORITY INFO: US 1991-650040 19910204
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1992-300037 [36]

AB The sequences given in Q27465-7 are probes which were used in the isolation of a synthetic HSA gene and in the construction of the expression cassette of the invention in plasmid pHSA211. The HSA gene (see Q27462) was cloned in the plasmid pMET-HSA. Mutagenising oligonucleotides were used to introduce and delete restriction sites to facilitate further cloning. The HSA gene was then cloned into plasmid M13mp10 to give vector pHSA101. A termination codon was introduced to the 3' of the HSA gene. The HSA gene was then cloned into plasmid pAO203, which is a plasmid containing the alpha-mating factor (AMF) **pre-pro sequence** (see Q27463). The resulting plasmid contained DNA encoding the 83-amino acid leader sequence of the AMF **pre-pro region** followed by the processing sites, Lys-Arg and (Glu-Ala)₂, joined to the DNA encoding the HSA gene. The (Glu-Ala)₂ processing site was then deleted and the pre-pro AMF-HSA **fusion** was then cloned into the Pichia pastoris vector pAO856. This resulted in the production of an expression cassette encoding the pre-pro AMF-HSA **fusion** gene under the control of the P. pastoris AOX1 promoter and regulatory regions, as well as the AOX1 transcription termination and polyadenylation signals

L3 ANSWER 130 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q27465 DNA DGENE
 TITLE: DNA fragment for prodn. of human serum albumin - comprises expression cassette including promoter and terminator sequences of methanol responsive gene, for expression in methylotrophic yeast
 INVENTOR: Davis G R; Provow S A
 PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNOLOGY IND ASSOC
 PATENT INFO: WO 9213951 A 19920820 75p
 APPLICATION INFO: WO 1992-US1015 19920204
 PRIORITY INFO: US 1991-650040 19910204
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1992-300037 [36]

AB The sequences given in Q27465-7 are probes which were used in the isolation of a synthetic HSA gene and in the construction of the expression cassette of the invention in plasmid pHSA211. The HSA gene (see Q27462) was cloned in the plasmid pMET-HSA. Mutagenising oligonucleotides were used to introduce and delete restriction sites to facilitate further cloning. The HSA gene was then cloned into plasmid M13mp10 to give vector pHSA101. A termination codon was introduced to the 3' of the HSA gene. The HSA gene was then cloned into plasmid pAO203, which is a plasmid containing the alpha-mating factor (AMF) **pre-pro sequence** (see Q27463). The resulting plasmid contained DNA encoding the 83-amino acid leader sequence of the AMF **pre-pro region** followed by the processing sites, Lys-Arg and (Glu-Ala)₂, joined to the DNA encoding the HSA gene. The (Glu-Ala)₂ processing site was then deleted and the pre-pro AMF-HSA **fusion** was then cloned into the Pichia pastoris vector pAO856. This resulted in the production of an expression cassette encoding the pre-pro AMF-HSA **fusion** gene under the control of the P. pastoris AOX1 promoter and regulatory regions, as well as the AOX1 transcription termination and polyadenylation signals

L3 ANSWER 131 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q25185 DNA DGENE
 TITLE: New proteins comprising active protein and integrin-affinity sequence - are antithrombotics useful in treating and

preventing myocardial infarction, stroke, pulmonary embolism
and deep vein thrombosis
INVENTOR: Dawson K M; Edwards R M; Fallon A
PATENT ASSIGNEE: (BRBI-N)BRITISH BIO-TECHNOLOGY LTD
PATENT INFO: WO 9207874 A 19920514 101p
APPLICATION INFO: WO 1991-GB1860 19911023
PRIORITY INFO: GB 1990-23149 19901024
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-183627 [22]

AB The sequence given is the yeast expression vector pSW6. It is based on the 2 micron circle from *Saccharomyces cerevisiae*. It is a shuttle vector capable of replication in both *S. cerevisiae* and *Escherichia coli* as it contains the origin of replication for both organisms. It also contains the *leu2* gene (a yeast selectable marker) and the ampicillin resistant locus for selection of plasmid maintenance in *E. coli*. This vector has enhanced ability for passage through *E. coli* and this greatly facilitates genetic manipulation with this vector. pSW6 contains an alpha-factor pre-pro peptide fused in-frame to epidermal growth factor (EGF). The expression of this fusion is under the control of an efficient galactose regulated promoter which contains hybrid DNA sequences from the *S. cerevisiae* GAL 1-10 promoter and the *S. cerevisiae* phosphoglycerate kinase (PGK) promoter. Transcription is terminated in this vector by the natural yeast PGK terminator. The EGF gene in pSW6 can be removed by digestion with HindIII and BamHI. This removes DNA encoding both EGF and 5 amino acids from the C-terminus of the alpha-factor pro-peptide. Genes to be inserted into the pSW6 expression vector must therefore have the general composition: HindIII site-alpha-factor adapter-gene-BamHI site

L3 ANSWER 132 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q21858 DNA DGENE

TITLE: Improved expression of peptide(s) as fusion proteins - using heterologous carrier with high isoelectric point for sepn. of peptide

INVENTOR: Tarnowski S J; Hilliker S; Willett W S
PATENT ASSIGNEE: (CALB-N)CALIF BIOTECHN INC
PATENT INFO: WO 9202550 A 19920220 50p
APPLICATION INFO: WO 1991-US5617 19910807
PRIORITY INFO: US 1990-564259 19900807
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-080032 [10]

AB This DNA sequence encodes a fusion protein comprising the *E. coli* beta-gal leader peptide fused to pro-ANP. A Staph V8 protease cleavage site is present in the fusion protein at the junction between the pro-sequence and the mature ANP sequence. Other Staph V8 cleavage sites in the protein, including the one between amino acids 13 and 14 of the leader peptide, were removed by changing the Glu codons in the fused gene to Gln codons. Human pro-ANP pro-sequence modified in this way is the preferred "carrier protein" for use in the production of other proteins, besides mature ANP. See also Q21857 and R21678

L3 ANSWER 133 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q21857 DNA DGENE

TITLE: Improved expression of peptide(s) as fusion proteins - using heterologous carrier with high isoelectric point for sepn. of peptide

INVENTOR: Tarnowski S J; Hilliker S; Willett W S
PATENT ASSIGNEE: (CALB-N)CALIF BIOTECHN INC
PATENT INFO: WO 9202550 A 19920220 50p
APPLICATION INFO: WO 1991-US5617 19910807
PRIORITY INFO: US 1990-564259 19900807
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-080032 [10]

AB This DNA sequence encodes a fusion protein comprising the *E. coli* beta-gal leader peptide fused to pro-ANP. Staph V8 protease cleavage sites are present in the fusion protein at the junction between the leader and the pro-sequence and between the pro-sequence and the mature ANP sequence. Other cleavage sites in the protein were removed by changing the Glu codons in the pro-sequence of the fused gene to Gln codons. Human pro-ANP pro-sequence modified in this way is the preferred "carrier protein" for use in the production of other proteins, besides mature ANP. See also Q21858 and R21678

L3 ANSWER 134 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1992N-Q20907 DNA DGENE
TITLE: Nucleic acid sequences for production of CD4 chimeric protein
- used to transfect streptomyces, contg. LTI signal sequence
linked to **pro-peptide** sequence
facilitating peptide cleavage
INVENTOR: Brawner M E; Fornwald J A; Arthos J
PATENT ASSIGNEE: (SMIK)SMITHKLINE BEECHAM
PATENT INFO: WO 9200985 A 19920123 47p
APPLICATION INFO: WO 1991-US4663 19910701
PRIORITY INFO: US 1991-665218 19910305
US 1990-551584 19900711
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1992-056814 [07]

AB The sequence was obtd. by sequencing the plasmid vector V1V2-hCH2-KA. Plasmid V1V2-hCH2strept was transformed into *S. lividans* strain 1326 and transformants selected. V1V2-hCH2-KA was expressed at 14mg/l. The plasmid construct contains a CD4 chimera (V1V2) in which the carboxy terminal portion of the encoded protein consists of a murine immunoglobulin light chain constant region. This sequence is operably linked to the coding sequence of the signal peptide of *Streptomyces* LTI, modified at its 5' end by the addition of bases encoding Lys-Arg. Also included in the expression vector is the sequence encoding an IgG1 constant region comprising the hinge and CH2 motifs. Human IgG1 is the most effective immunoglobulin subclass at mediating cell killing by both complement and ADCC. The vectors are used for the prodn. of sol. CD4 chimeric proteins in bacterial hosts, in which the HIV gp120 binding region is joined to a region of the human Ig constant region lacking the CH3 domain, which increases the stability of the CD4, thus increasing the serum half life and/or potency against HIV infection and inhibit virus-induced cell **fusion**, relative to soluble CD4. See also Q20908,9

L3 ANSWER 135 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1991N-Q13197 DNA DGENE
TITLE: DNA constructs for secretion of foreign proteins - using
signal sequence and portion of BAR1 C-terminal domain to
direct secretion
INVENTOR: Welch S K; Mackay V L; Yip C L
PATENT ASSIGNEE: (ZYMO-N)ZYMOGENETICS INC
PATENT INFO: US 5037743 A 19910806 40p
APPLICATION INFO: US 1988-270933 19881114
PRIORITY INFO: US 1988-270933 19881114
US 1987-104316 19871002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-252061 [34]

AB By combining the BAR1 putative signal sequence (tag a) with the coding region for amino acids 423-526 (tag b) of the third (C-terminal) domain of the BAR1 gene, secretion levels for TGF greater than those obtd. using analogous constructs comprising the MEalpha pre-**pro sequence** are obtd. The hybrid secretory peptide directs the secretion of heterologous proteins or polypeptides, e.g. urokinase, insulin, platelet-derived growth factor, epidermal growth factor or transforming growth factor alpha. See also Q13195-7

L3 ANSWER 136 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1991N-Q13196 DNA DGENE
TITLE: DNA constructs for secretion of foreign proteins - using
signal sequence and portion of BAR1 C-terminal domain to
direct secretion
INVENTOR: Welch S K; Mackay V L; Yip C L
PATENT ASSIGNEE: (ZYMO-N)ZYMOGENETICS INC
PATENT INFO: US 5037743 A 19910806 40p
APPLICATION INFO: US 1988-270933 19881114
PRIORITY INFO: US 1988-270933 19881114
US 1987-104316 19871002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-252061 [34]

AB By combining the BAR1 putative signal sequence (tag a) with the coding region for amino acids 391-526 (tag b) of the third (C-terminal) domain of the BAR1 gene, secretion levels for TGF greater than those obtd. using analogous constructs comprising the MEalpha pre-**pro sequence** are obtd. The hybrid secretory peptide directs the secretion of heterologous proteins or polypeptides, e.g. urokinase, insulin, platelet-derived growth factor, epidermal growth factor or transforming growth factor alpha. See also Q13195-7

L3 ANSWER 137 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1991N-Q12154 DNA DGENE
TITLE: **Fusion** protein cleavage by blood clotting enzyme -
for prodn. of fractions having greater antithrombotic
activity for therapy and prophylaxis
INVENTOR: Dawson K M; Hunter M G; Czapleswski L G
PATENT ASSIGNEE: (BRBI-N)BRIT BIO-TECHN LTD
PATENT INFO: WO 9109125 A 19910627 115p
APPLICATION INFO: WO 1990-GB1911 19901207
PRIORITY INFO: WO 1990-GB1911 19901207
GB 1989-27722 19891207
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-208151 [28]
AB The vector is based on the 2u circle from *S. cerevisiae*. It is deposited
in *S. cerevisiae* strain BJ2168 as NCIMB 40326. It is a shuttle vector
capable of replication in both *E. coli* and *S. cerevisiae* and contains
origins of replication for both, the *leu2* gene (selectable marker), and
an ampicillin resistant locus. The *E. coli* sequences are derived from *E.*
coli ColE1-based replicon pAT153. The vector contains an alpha factor
pre-pro-peptide gene fused in frame to the gene for
epidermal growth factor (EGF). The expression of this **fusion**
is under control of a galactodse regulated promoter which contains hybrid
DNA from *S. cerevisiae* GAL 1-10 promoter and the *S. cerevisiae*
phosphoglycerate kinase (PGK) promoter. The EGF gene can be excised by
digestion with HindIII and BamHI. The plas- mid was used for the
expression of a synthetic hirudin HV-1 gene in *E. coli* K12 HW87. The
plasmid can be used to construct ex- pression vectors in which the
hirudin gene is linked to a second gene encoding e.g. another hirudin
protein, streptokinase or a streptokinase-like protein, via a linking
peptide. This peptide link contains a cleavage site for e.g. factor X or
thrombin which can be cleaved, releasing the individual proteins which
have anti- thrombotic activity. The enzymes which cleave the
fusion protein are present at the site of the target thrombus so
the active agents are released specifically at the place where clot
formation is occurring. See also Q12153-Q12156, Q12158-Q12162 and Q12490

L3 ANSWER 138 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991N-Q12039 DNA DGENE
TITLE: New recombinant protein complexes having factor VIIIC
activity - used to produce antibodies, to isolate von
Willebrand factor in diagnostic assays and to treat
haemophilia
INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
(CHIR-N) CHIRON CORP
PATENT INFO: WO 9107490 A 19910530 56p
APPLICATION INFO: WO 1990-DK291 19901115
PRIORITY INFO: US 1989-438639 19891117
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-178102 [24]
AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain
(see Q12035). The light chain gene is fused directly to the tPA signal
sequence. This allows independent secretion of the 80K glycoprotein but
also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser
to create a tPA signal sequence cleavage site. In pSVF8-80A the Ser codon
is changed to a Glu codon and 7 codons encoding the putative tPA
pro-peptide are deleted. Cleavage by signal peptidase
releases non-mutant FVIII:C light chain

L3 ANSWER 139 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991N-Q12038 DNA DGENE
TITLE: New recombinant protein complexes having factor VIIIC
activity - used to produce antibodies, to isolate von
Willebrand factor in diagnostic assays and to treat
haemophilia
INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
(CHIR-N) CHIRON CORP
PATENT INFO: WO 9107490 A 19910530 56p
APPLICATION INFO: WO 1990-DK291 19901115
PRIORITY INFO: US 1989-438639 19891117
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1991-178102 [24]
AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain
(see Q12035). The light chain gene is fused directly to the tPA signal
sequence. This allows independent secretion of the 80K glycoprotein but
also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser

to create a tPA signal sequence cleavage site. In pSVF8-80R the Ser codon is changed to a Glu codon and the 3 codons corresponding to the tPA **pro-peptide** are deleted. This construction was made in the hope that cleavage by a Golgi-resistant protease with dibasic specificity would release FVIII:C light chains having Glu amino terminal

L3 ANSWER 140 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1991N-Q12037 DNA DGENE
 TITLE: New recombinant protein complexes having factor VIIIC activity - used to produce antibodies, to isolate von Willebrand factor in diagnostic assays and to treat haemophilia
 INVENTOR: Chapman B; Burke R; Rasmussen M E; Mikkelsen J M
 PATENT ASSIGNEE: (NOVO)NOVO NORDISK A/S
 (CHIR-N) CHIRON CORP
 PATENT INFO: WO 9107490 A 19910530 56p
 APPLICATION INFO: WO 1990-DK291 19901115
 PRIORITY INFO: US 1989-438639 19891117
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-178102 [24]

AB Plasmid pSVF8-80 is an expression plasmid for the Mr. 80 K FVIII-LC chain (see Q12035). The light chain gene is fused directly to the tPA signal sequence. This allows independent secretion of the 80K glycoprotein but also substitutes the N-terminal Glu residue of mature FVIII:C with a Ser to create a tPA signal sequence cleavage site. In pSVF8-80S the Ser codon is changed to a Glu codon and the 12 codons corresponding to amino acids -12 to -1 of the tPA pre-**pro-region** are deleted. Cleavage of the truncated signal peptide releases non-mutant FVIII:C light chain

L3 ANSWER 141 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1991N-Q11567 DNA DGENE
 TITLE: Recombinant prodn. of CD4 in Pichia pastoris - where CD4 contains site of interaction between CD4 and HIV and is used to treat and prevent AIDS
 INVENTOR: Buckholz R G; Brierley R A; Odiorne M S; Siegel R S; Wondrack L M
 PATENT ASSIGNEE: (SALK)SALK INST BIOTECHN
 PATENT INFO: WO 9105057 A 19910418 64p
 APPLICATION INFO: WO 1990-US5520 19900927
 PRIORITY INFO: US 1989-413938 19890928
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1991-132862 [18]

AB An EcoRI-XbaI fragment was excised from a 2.2 kb linear BglII-NheI DNA fragment containing a segment encoding the first variable region of CD4 accompanied by flanking DNA from E.coli. The excised fragment was ligated to plasmid pIBI25 (containing an fl ORI and a T7 promoter) to give plasmid pSCD4. Digestion with XbaI and EcoRI showed a 477bp fragment contained the V1 region. This fragment was isolated and ligated to a plasmid containing the pre-**pro sequence** from yeast alpha-mating factor (AMF). Mutagenesis was performed to fuse the AMF pre-**pro sequence** directly to the V1 coding region. An EcoRI linker was added to the 3' end of the AMF pre-pro-V1 insert prior to digestion with EcoRI to give a 560bp fragment. The fragment was ligated to EcoRI-digested pAO815 (containing AOX1 transcription terminator) and the ligation mixture transformed into MC1061 cells. Plasmid pSCD103 was isolated from the transformants. See also Q11566

L3 ANSWER 142 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1990N-Q06748 DNA DGENE
 TITLE: New DNA fragment for expressing epidermal growth factor - in methylotrophic yeast, contg. host derived promoter and terminator and S. cerevisiae pre-**pro sequence**
 INVENTOR: Siegel R S; Buckholz R G; Thill G P; Wondrack L M
 PATENT ASSIGNEE: (SALK)SALK INST BIOTECHNO
 PATENT INFO: WO 9010697 A 19900920 57p
 APPLICATION INFO: WO 1990-US1353 19900315
 PRIORITY INFO: WO 1990-US1353 19900315
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 1990-305021 [40]

AB The probe was used to screen for transformants contg. pPG4.0 which carries the primary alcohol oxidase gene (AOX1) and regulatory regions. The sequence contains the AOX1 promoter up to, but not including the ATG initiation codon, fused to the sequence of an EcoRI linker. The promoter was used to direct expression of a new **fusion** gene made by

ligating the alpha mating factor pre-**pro** sequence
(including the proteolytic processing site Lys-Arg) to the code for the
human epidermal growth factor in plasmid pEGF819. See also Q06749

L3 ANSWER 143 OF 143 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1984N-N40016 DNA DGENE

TITLE: Human insulin-like and epidermal growth factors - prepd. by
cultivation of recombinant hosts

INVENTOR: Lee J M; Ullrich A

PATENT ASSIGNEE: (GETH)Genentech Inc

PATENT INFO: EP 128733 A 19841219 68p

APPLICATION INFO: EP 1984-303783 19840605

PRIORITY INFO: US 1983-501353 19830606

US 1983-506078 19830620

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1984-314109 [51]

AB The DNA encodes a **fusion** protein comprising human insulin-like
growth factor-1 (hIGF1) fused to alpha factor pre-**pro**
sequence. The hIGF1 is cleaved from the **fusion** protein
using the collagenase recognition site situated at the N-terminal of the
mature hIGF1 sequence. The **fusion** protein is expressed by
inserting the DNA into an expression vector and using this to transform a
host cell. hIGF1 is useful for the prophylaxis or treatment of growth
conditions

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	6.66	9.51
DISPLAY CHARGES	517.66	517.66
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FULL ESTIMATED COST	524.32	527.17

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	524.32	527.17

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